Vol. 12 No. 4 OCTOBER, 1958

UNIVERSITY OF MICHIGAN
1959
PUBLIC HEALTH LIBRARY

BRITISH JOURNAL OF PREVENTIVE & SOCIAL MEDICINE

EDITED BY
THOMAS McKEOWN AND IAN TAYLOR

WITH THE ASSISTANCE OF

W. MELVILLE ARNOTT
F. A. E. CREW
A. BRADFORD HILL
LANCELOT HOGBEN
W. J. E. JESSOP
AUBREY LEWIS
W. P. D. LOGAN
J. N. MORRIS
J. A. FRASER ROBERTS
A. C. STEVENSON
ALICE M. STEWART
THE EDITOR OF THE *British Medical Journal*

CONTENTS

PAGE

Married Women who Work: Their Own and Their Children's Health. Ann Cartwright and Margot Jefferys 159

Sickness, Change of Residence, and Death. I. General Results of Follow-up in Two Population Groups. D. J. Thompson and A. Ciocco 172

Genotypic Frequencies among Close Relatives of Propositi with Conditions determined by X-Recessive Genes. G. Knox 183

On the Nature of Determinants of Congenital Pyloric Stenosis. G. Knox 188

An Estimate from Pedigree Data of the Gene Frequency for Colour Blindness. G. Knox 193

Seasonal Swing in Mortality in England and Wales. A. Kanellakis 197

Arterial Blood Pressure in Plantation Workers in North East India. J. M. G. Wilson .. 204

Index for 1958 210

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION (4 NUMBERS) £3 U.S.A. $10.00 SINGLE NUMBER 17s. 6d.

NOTICE TO CONTRIBUTORS

THE BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE is intended for the publication of original work in the field. Contributions in the English language from workers of any nationality may be considered for publication.

As understood by those who are responsible for this Journal, social medicine is that branch of science which is concerned with: (*a*) biological needs, interactions, disabilities, and potentialities of human beings living in social aggregates; (*b*) numerical, structural, and functional changes of human populations in their biological and medical aspects. To a large extent its methods must necessarily be statistical, involving the use of numerical data obtained either from official sources or from special field investigations, and interpreted in the light of established findings of the laboratory and of the clinic. Social medicine takes within its province the study of all environmental agencies, living and non-living, relevant to health and efficiency, also fertility and population genetics, norms and ranges of variation with respect to individual differences, and investigations directed to the assessment of a regimen of positive health.

All papers submitted for publication and all other editorial matters should be addressed to The Editors, BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE, c/o British Medical Association, Tavistock Square, London, W.C.1.

Papers are accepted on the understanding that they are subject to editorial revision, and that they are contributed to this Journal only. The Editors cannot undertake correspondence about papers returned as unsuitable on the advice of members of the Editorial Board.

Adequate reference should be made to previous work on the subject of the paper. A summary of observations and conclusions must be given.

Papers sent for publication must be typewritten on one side of the paper only, with double spacing and with a margin of at least 1½ inches. Illustrations should be used sparingly. Photographs should be printed on glossy paper and should be a little larger than the size desired for reproduction. Drawings and diagrams should be done in black ink on tracing linen, Bristol board, or stout, white paper. Any lettering on these drawings should be lightly inserted in pencil. The setting up of type by the printers will be much facilitated if attention is paid to the proportions of the standard page measurements. The Editors express the hope that contributors will study the conventions of shading and design of charts employed in the Journal with a view to standardizing visual symbols for ready recognition.

References should be arranged alphabetically at the end of the paper according to the Harvard system. If the reference is to a book, the place of publication, the number of the edition, and the page number should be given. In the text the year of publication must follow the author's name, more than one paper in any one year being indicated by a small letter (a, b, c) after the date. The reference should be given as follows: author's name, initials, year of publication (in parentheses), title of periodical (in italics, abbreviated according to *World Medical Periodicals*), volume number (bold type arabic numerals), and first page number (ordinary type arabic numerals); book titles (in roman and inverted commas), followed by publisher, place of publication, etc.:

Engle, E. T., and Shelesnyak, M. C. (1934). *Hum. Biol.*, **6**, 431.
Fluhmann, C. F. (1936). *Amer. J. Obstet. Gynec.*, **31**, 573.
—— (1939). " Menstrual Disorders." W. B. Saunders, Philadelphia.
Gómez, F. D. (1942). *Hoja tisiol.*, **2**, 25.

Contributors will receive one proof, but it is assumed that all but verbal corrections will have been made in the original manuscript; an allowance at the rate of ten shillings per sheet of sixteen pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Twenty-five reprints of papers will, if desired, be provided free. A limited number of additional reprints at cost price can be supplied if application is made when returning proofs. An estimate of the cost will be given on application to the Publishing Manager, British Medical Association.

The Journal will be published quarterly.

Papers which have appeared in THE BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE remain the property of the Journal, and permission to republish them must be obtained from the Editors.

Applications for advertisement space should be addressed to the Advertisement Manager, British Medical Association, Tavistock Square, London, W.C.1.

NOTICE TO SUBSCRIBERS

Subscriptions (£3 per annum) are payable to the British Medical Association.

Brit. J. prev. soc. Med. (1958), **12**, 159–171

MARRIED WOMEN WHO WORK: THEIR OWN AND THEIR CHILDREN'S HEALTH

BY

ANN CARTWRIGHT

Department of Public Health and Social Medicine, University of Edinburgh,

AND

MARGOT JEFFERYS

London School of Hygiene and Tropical Medicine, University of London

Estimates of the proportion of married women who are doing paid work outside their homes vary considerably; but, despite the difficulties of securing reliable figures, it seems safe to conclude that, in most parts of the United Kingdom, the proportion is much greater to-day than it was before the second world war. In the 1931 Census for England and Wales, for example, only 11 per cent. of the married women were enumerated as gainfully employed or insured and seeking work compared with 22 per cent. in the 1951 Census. Subsequent estimates suggest that the proportion is still rising and that, nationally, about one in every four married women undertakes paid work outside her home.

Much emotion and not a little moralizing has been generated by this change; but there is a dearth of information on the circumstances of those who work. For example, it is not known how many of those who work have children; nor are there any routine administrative statistics which show how many children at any given age have mothers in full or part-time work.

When there is so little information upon the dimensions of the problem, it is not surprising to find that there is almost no attempt to assess objectively the effects which working outside their home has on married women and on their children. Almost the only study to throw light on the health of children under 5 years old whose mothers were in full- or part-time employment is that of Douglas and Blomfield (1958), which relates to children born in 1946.

The present paper presents some material which is relevant to this problem.

Methods

The data were obtained in the course of an inquiry undertaken by the public Health Department of the London School of Hygiene and Tropical Medicine during the years 1954–57. The inquiry concerned a post-war housing estate built to rehouse Londoners in Hertfordshire. The population numbered about 17,000, and was composed of a relatively high proportion of young married couples with children and few elderly people. There were no factories on the estate; local employment opportunities for women were almost entirely restricted to the few shops on the estate and the public services.

Most of the information contained in this paper relates to families and individuals living in a randomly selected three-sixteenths of the dwellings on this estate. It came from three main sources: first, from the adults in this sample of dwellings, who were interviewed in their own homes; secondly, from the records of the general practitioners with surgeries on the estate, and thirdly, from the school teachers in the area. Further information about the children who had a routine school medical examination between January and March, 1957, was provided by their parents and school teachers.

In the interview survey, we tried to question all the adults* in our sample of dwellings twice, with an interval of 4 weeks between the two interviews. Mothers were interviewed about children of school age or less on two further occasions, also at an interval of 4 weeks. Two interviews were completed for 81 per cent. of the 3,040 individuals in our sample, and one interview for another 5 per cent. leaving 14 per cent. with no interview†. The information recorded on standard schedules, covered very generally the health of the individuals concerned, their use of the various branches of the health services, their jobs and educational background, and certain other social characteristics.

* Adults were defined as people aged 15 and over who had left school.

† The effect of this failure rate is discussed elsewhere.

The information obtained from general practitioners' records, kept specially for the purpose, included a count of the number of consultations which those who were registered with one of the six doctors on the estate had made during a calendar year (Brotherston, Chave, and others, 1956). About 86 per cent. of those living in the sample dwellings were registered with one or other of these doctors.

The information which the school teachers were asked to provide related to those children in the sample dwellings who were at school on the estate at the time of the 1954–55 inquiry. With few exceptions, the children attending infant, junior, and secondary modern schools went to estate schools; but all those attending grammar, technical, special, or private schools went elsewhere. The teachers' information, therefore, covered only 76 per cent. of the school children in the sample, but 88 per cent. of those at school on the estate*. The teachers assessed scholastic ability and attainments, certain aspects of personality, parental care, and attitude to the school. Estate schools also kept termly records of the heights and weights of all their pupils, and these records, together with further information from parents and teachers, were available for children who had a routine school medical examination during the January term, 1957.

Results

Employment of Married Women

At the time of our survey, some 40 per cent. of the married women were "gainfully employed"†: 18 per cent. were in what we called "full-time" work, that is, a job of 30 or more hours a week outside the home, 17 per cent. were working outside their homes for less than 30 hours per week, and 5 per cent. were gainfully employed in their own homes. For the purposes of the subsequent analysis we have grouped these two latter categories together, and called them "part-time" workers. We should stress, in addition, that our data relate to a point in time and do not take into account the fact that married women are likely to move in and out of employment with greater frequency than other categories of workers.

The proportion of married women at work was greatest among those in the middle age groups. Only one-third of those under 35 worked, compared with nearly half of those aged 35–54. But, as Table I shows, the proportion of those doing part-time work increased with advancing age.

Table I

PERCENTAGE EMPLOYMENT OF MARRIED WOMEN, BY AGE

Employment	Age (yrs)				
	Under 35	35–44	45–54	Over 55	All Ages
Working: Full-time	17	21	15	3	18
Working: Part-time	15 } 32	28 } 49	31 } 46	19 } 22	22 } 40
Not Working	68	51	54	78	60
Sample (=100 per cent.)	232	214	78	31	555

Nearly nine out of every ten of the male tenants of this estate worked at skilled manual occupations classified by the Registrar General in Social Classes III, IV, and V. The distribution of married women's occupations as between manual and non-manual was very similar. Among both full-timers and part-timers manual work predominated; but a larger proportion of the part-timers than of the full-timers was in completely unskilled or semi-skilled work (Table II). Since there was no significant difference in the type of school which the full-time and part-time workers had attended or the age at which they had left school, we concluded that the difference in the type of work obtained was more likely to be a reflection of the work available than of different levels of skill or training.

Table II

OCCUPATIONS OF MARRIED WOMEN AT WORK, BY SOCIAL CLASS

Social Class (Registrar General's Classification)	Full-time Workers (per cent.)	Part-time Workers (per cent.)
I and II Professional and Intermediate ..	8	2
III Clerical	15	6
III Distributive	15	9
III Other Skilled Manual	24	22
IV Semi-skilled Manual	25	36
V Unskilled Manual	13	25
Sample (=100 per cent.)	98	124

An analysis of the workplaces of full-timers and part-timers lends substance to this view. A larger proportion of the part-timers were found to be

* A time lag between the house-to-house inquiry and the request for information from teachers was chiefly responsible for the failure to secure a schedule for each child.

† Widows and those living apart from their husbands are not included in this analysis.

working on the estate itself and within a 4-mile radius (Table III).

TABLE III

PLACES OF WORK OF MARRIED WOMEN AT WORK

Place of Work*	Full-time Workers (per cent.)	Part-time Workers (per cent.)
On Estate	16	29
Within 4 miles of Estate	57	62
More than 4 miles from Estate	27	9
Sample (= 100 per cent.)	98	98

* Excluding those working in their own homes

Our analysis showed that the question whether a married woman went out to work was closely associated with whether she had children. Nearly two-thirds of those without children worked, the great majority of them full-time, whereas the proportion of those who worked who had at least one child was rather less than 40 per cent. There was little difference between the proportions working amongst those with one, two, or three children; but amongst those with four or more children rather fewer than one-third were working and only one-tenth were working full-time (Table IV).

TABLE IV

PERCENTAGE EMPLOYMENT OF MARRIED WOMEN, BY NUMBER OF CHILDREN

Employment	Number of Children				
	None	One	Two	Three	Four or More
Working: Full-time	55	10	20	14	10
Working: Part-time	10	29	22	23	22
Working (total)	65	39	42	37	32
Not Working	35	61	58	63	68
Sample (= 100 per cent.)	42	98	167	137	103

There was also a low proportion of full-timers among mothers of only children. The reason for this would seem to be that such mothers were more likely to have a child of pre-school age than mothers of two or three children. Table V indicates that the most significant determinant of whether or not a mother worked was the age of the youngest child living at home.

Few mothers of very young children went out to work. In our sample, there were only two mothers of children under 2 years old in full-time employment and two in part-time work. Among mothers whose youngest children were between 2 and 5 years old, about one-sixth were working, the majority part-time. The really decisive change came when the youngest child was of primary school age. Of such mothers, in contrast to those with pre-school children, no fewer than half were working. Amongst mothers with youngest children of secondary school age (10 to 14) nearly two-thirds were working, and an increasing proportion of the workers undertook full-time work. There were fewer mothers working among those who had at least one unmarried child who had left school but continued to live at home. Possibly the extra income which these children brought to the household made it less urgent for the mother herself to work, and in addition she herself would be older.

TABLE V

PERCENTAGE EMPLOYMENT OF MOTHERS, BY AGE OF YOUNGEST UNMARRIED CHILD LIVING AT HOME

Mothers' Employment	Age of Youngest Child (yrs)				
	Under 2	2–4	5–9	10–14*	15 or Over*
Working: Full-time	3	6	16	29	22
Working: Part-time	3	11	37	37	20
Not Working	94	83	47	34	58
Sample (= 100 per cent.)†	71	123	183	59	40

* The 10 to 14 year group includes three mothers whose youngest child was 15 and still at school. The 15 and over group includes no mothers whose youngest children were still at school.

† Excludes mothers in households where there were two or more mothers of dependent children.

In other words, the working mother with a child of pre-school age was, in 1954–55, a comparative rarity; but the woman whose children had all reached compulsory school age was as likely to be at work as "not gainfully employed"; amongst mothers whose children had all reached secondary school age, the woman who did not work was the exception rather than the rule. When her children, in their turn, were all of an age to earn, the mother was more likely once again to become a housewife only.

CHILDREN WHOSE MOTHERS WORK

Douglas and Blomfield, in their national study of a sample of children born in 1946, found that, when the children were 2 years old, 7·5 per cent. of them had mothers at work. By the time they were 4 years old, 15·3 per cent. had mothers at work.

Our study covered children of all ages at a given point in time, and is not, therefore, comparable in all respects to the national inquiry. However, the proportion of children under 5 years old with a mother at work (Table VI, overleaf) is similar to that found in the earlier inquiry. School children of primary school age were much more likely than pre-school children to have a mother at work, and those of secondary school age even more so. Amongst these two latter groups, the chances that a child would have a mother at work depended very largely on his

TABLE VI

PERCENTAGE EMPLOYMENT OF MOTHERS, BY AGE OF CHILDREN

Mothers' Employment	Age of Children (yrs)			
	Under 2	2–4	5–9	10 or More
Working { Full-time	3	5	10	20
Working { Part-time	4	9	27	33
Not Working	93	86	63	47
Sample (= 100 per cent.)	67	186	394	281

position in the family. For example, in the 5 to 9 year age group (Table VII), younger children in families of two were twice as likely to have a mother at work as older children (57 per cent. as against 28 per cent). In the same age group, amongst children who came from families with three children, only 12 per cent. of the oldest children had mothers at work compared with 31 per cent. of middle children and 65 per cent. of youngest children. Clearly, in this age group, the children most likely to be affected are the youngest children in the families of two or three. So, although older children or those from large families have to compete with their siblings for their mother's attention, they are much less likely than their younger siblings to have a mother at work; that is, with demands on her time and energy outside the family.

CHILD HEALTH AND THE WORKING MOTHER

Douglas and Blomfield were not able to find many consistent differences between the illness records during the first 5 years of life of children whose mothers had worked full-time or part-time for more than a year and those of children whose mothers had not worked at all. There was an excess of lower respiratory tract infections among the children of those full-time workers who used the day nurseries during the first 2 years of life; but there were no indications of excessive illness among the children of those who worked full-time but did not use the day nurseries. Nor did the groups of children differ in heights or in liability to accidents. There was no excess of bad habits or nightmares at 6 years old among the children of full-time workers, and the apparent excess of bed-wetting amongst such children was wholly explained by the relatively high proportion of broken homes amongst them.

The small number of children under 5 years old in our sample whose mothers were working full-time or part-time makes it difficult to compare their health records with those of children whose mothers did not work. More reliance can be placed on the comparisons between children of school age.

Table VIII (opposite) shows, for children in three age groups, the varying proportions reported by their mothers to be suffering from or liable to certain symptomatic conditions. It also shows the average number of illnesses reported by their mothers to be present at the time of interview or to be recurring.

This information, collected quite differently from that obtained by Douglas and Blomfield, also fails to reveal any excess of illness among the children of school or pre-school age with mothers at work. The slight variations in the proportions reporting no illness and in the average numbers of illnesses reported can be explained by chance.

The types of condition reported for the different groups of children were also fairly similar. Only catarrh had larger variations than would be expected to arise purely by chance. A possible explanation for this finding is that mothers—especially mothers of pre-school children—are not likely to undertake full-time work unless their children are relatively free from chronic upper respiratory tract infections. The excess of eye-strain among the children of full-time workers, which was significant among the 5 to 9 year olds, may be associated with reading or televiewing habits. These children were regarded by their teachers as being rather more intelligent than the children of mothers who did not work (see Tables XIV and XV), and it is possible that, in 1954–55, there were more television sets in the homes of families where the mother was working than in those where she was not. Our data,

TABLE VII

PERCENTAGE EMPLOYMENT OF MOTHERS, BY CHILD'S POSITION IN FAMILY AND SIZE OF FAMILY, FOR AGE GROUP 5 TO 9 YEARS

Mothers' Employment	Number of Children						
	2		3			4 or More	
	Older	Younger	Oldest	Middle	Youngest	Older	Middle or Younger
Working { Full-time	9	18	—	5	24	2	5
Working { Part-time	19 } 28	39 } 57	12 } 12	26 } 31	41 } 65	10 } 12	25 } 30
Not Working	72	43	88	69	35	88	70
Sample (= 100 per cent.)	54	66	34	42	54	42	79

TABLE VIII

CHILDREN'S REPORTED ILL-HEALTH, BY MOTHERS' EMPLOYMENT

Age Group of Children (yrs)		Under 5		5–9			10 or More		
Mothers' Employment		Full- or Part-time	None	Full-time	Part-time	None	Full-time	Part-time	None
Average Number of Illnesses Reported		1·2	0·9	1·3	1·5	1·4	1·3	1·5	1·4
Number Reporting no Illness (per cent.)		35	45	32	26	26	33	23	30
Recurring Symptoms Reported (per cent.)	Catarrh	3	14	12	21	26	9	18	18
	Colds	13	24	24	20	26	22	11	20
	Coughing	29	14	15	17	17	7	5	9
	Eyestrain	10	5	20	9	9	11	9	8
	Headaches	3	1	10	7	9	13	20	15
	Loss of Appetite	10	8	5	13	9	—	4	3
	Nerves	6	6	12	18	12	15	26	11
	Rashes or Itches	6	4	15	4	7	5	5	4
	Running Ears or Earache	3	8	12	10	10	4	4	5
	Sore Throats	3	5	5	7	10	13	1	6
	Stomach Pains	3	2	7	10	6	5	8	9
	Trouble with Teeth or Gums	6	9	10	10	7	9	11	11
Sample (= 100 per cent.)		31	223	41	107	246	55	93	132

unfortunately, did not include this information. It is not easy to see why there should be more nerves and fewer colds and sore throats among children of part-time workers over 10 years old than among children of full-time workers and housewives.

CHILDHOOD HABITS AND PHOBIAS

It is equally difficult to explain why there should be more children with "nerves" among those whose mothers worked part-time than among those whose mothers worked full-time or not at all. Besides asking about the physical health of the children, we asked mothers of those over the age of 2 years whether their children had certain "bad" habits, such as thumb sucking, or were prone to nervous troubles such as nightmares. The conditions about which we asked specifically are enumerated in Table IX, together with the percentage of children for whom positive replies were given.

TABLE IX

CHILDREN'S REPORTED HABITS AND PHOBIAS, BY MOTHERS' EMPLOYMENT

Age Group of Children (yrs)		Children under 5		Children aged 5–9			Children aged 10 or More		
Mothers' Employment		Full- or Part-time	None	Full-time	Part-time	None	Full-time	Part-time	None
Percentage Children with Habit or Phobia	Thumb Sucking	23	13	16	10	13	9	3	8
	Nail Biting	12	16	20	25	19	29	26	21
	Nose Picking	8	12	5	22	8	—	4	2
	Twitches	—	1	2	9	3	4	1	2
	Stammering and Stuttering	—	8	9	8	2	4	3	2
	Temper Tantrums	8	18	5	11	9	9	10	3
	Too Quiet or Timid	4	2	2	3	4	5	4	4
	Nightmares or Night Fears	4	8	9	13	12	7	9	9
	Daytime Fears	—	3	2	3	5	—	—	1
	Excessive Rivalry or Jealousy	4	5	2	5	3	4	4	4
	Refusal to Eat an Adequate Diet	19	10	14	8	9	2	3	3
	Excessive Dislike of School*	—	—	—	6	4	2	3	5
	Poor Progress in Learning*	—	—	9	9	7	9	7	5
	Difficulty in making Friends of Same Age*	—	—	2	7	4	5	2	1
	Serious Disobedience*	—	—	—	1	2	2	4	2
	Bed Wetting*	—	—	9	7	8	2	1	3
	None of these Habits or Disorders	54	45	39	31	34	47	49	53
	Total (= 100 per cent.)	26	166	44	105	250	55	90	133
Average No. of Habits per Child		0·81	0·96	1·07	1·45	1·14	0·93	0·87	0·76

* Mothers were not asked about such conditions for children under 5 years of age.

The percentage of children reported by their mothers as having at least one of the conditions listed was greatest among the 5 to 9 year-olds. In this group but not in the others, the children of part-time workers were more frequently reported to have at least one of these conditions. The specific habits which they had more frequently than other children were nose picking, nail biting, and twitches. In the main, however, it is the similarity rather than the variation in the numbers reported by their parents as subject to these habits or phobias that is noteworthy. Like Douglas and Blomfield we could only conclude that there were no overt signs that children of any age whose mothers worked full-time or part-time were adversely affected emotionally.

Physical Development

The authors of the national inquiry (Douglas and Blomfield, 1958) found that there was no difference between the heights of children up to the age of 5 whose mothers worked and the heights of those whose mothers did not. Our information relates to children who had a routine medical examination between January and March, 1957, and for whom height and weight data were recorded (Table X).

There is no indication in our figures that the children of working mothers are of inferior stature. The slight differences in average height, in the proportions of weight for height, and in the rate of growth, were not statistically significant. In short, we confirm for children of school age the findings of Douglas and Blomfield for children under 5 years old.

School Attendance

Absence from school is an equivocal measure of ill-health among children. One child may have more absences than another for a variety of reasons. He may be more frequently ill, or he may have a mother who takes more precautions; yet again, his absences may be nearer to truancy, either connived at by the parents or not.

At our second interviews with mothers about the health of their children, we asked whether the child had been absent from school in the 4 weeks since the first interview. The results are shown in Table XI.

TABLE XI

PERCENTAGE OF CHILDREN ABSENT FROM SCHOOL FOR ONE OR MORE DAYS DURING A PERIOD OF 4 WEEKS, BY MOTHERS' EMPLOYMENT

Age Group of Children (yrs)	Mothers' Employment	Percentage Absent	No. of Children (= 100 per cent.)
5–9	Working { Full-time	20	40
	Part-time	25	104
	Not Working ..	31	238
10 or More	Working { Full-time	16	52
	Part-time	22	92
	Not Working ..	27	128

Children whose mothers worked full-time were least frequently absent from school, and those whose mothers did not work were most frequently absent. During the inquiry and before the results of the

TABLE X

CHILDREN'S PHYSICAL GROWTH AND STATURE, BY MOTHERS' EMPLOYMENT

School Attended			Infant and Junior		Secondary Modern	
Age Group of Children (yrs)			5 to 10		11 and Over	
Mothers' Employment			Working	Not Working	Working	Not Working
Measure of Physical Stature	(A) Average Height (in.)		49·5	48·7	61·0	60·6
	(B) Weight in relation to Height* (per cent.)	Heavy	5	13	17	17
		Average	86	76	62	56
		Light	6	11	21	27
	(C) Rate of Growth in Height† (per cent.)	Accelerated	2	2	13	17
		Normal	89	92	65	57
		Retarded	9	6	22	26
	Total Numbers (= 100 per cent.)	For Measures A and B	67	192	47	77
		For Measure C	46	125	45	70

* If children of any given height exceeded a certain weight they were classified as heavy. If they fell below a certain weight they were classified as light.

† Children's height gains at 6-monthly intervals were plotted on a chart against a curve representing the average height of London School children of the same sex and age in 1949. If the slope made by joining the points charted for the child at different ages from May, 1956, to May, 1957, was much steeper than the curve representing average heights of L.C.C. children, the child's growth was classified as "accelerated". If the slope was much less steep the child's growth was classified as "retarded". The greater proportion of secondary school children with accelerated or retarded growth rates (as compared with junior school) may reflect the different ages at which children reach puberty, which often appears to be preceded by a spurt in height.

family interviews were known, school teachers had expressed their concern about the number of children who were sent to school when they were clearly unwell. The teachers were convinced that the children most concerned were those whose mothers were working. Our findings may be taken as a partial confirmation of their impressions, at least in so far as the absences of children of mothers who were working and "not gainfully employed" were concerned. Our data will not, however, allow us to confirm or deny that the children of mothers who worked were more frequently sent to school when unwell than those whose mothers stayed at home. The proportion of children recorded as absent during a 4-week period seems high, particularly among those aged 10 years or more. There was no epidemic of an infectious disease during our family health survey which could account for a high absence rate. Another explanation, equally difficult to prove or disprove, is that working mothers are more ambitious for themselves and their families and, therefore, more concerned than non-working mothers that their children should attend school regularly. Still another possibility is that mothers who do not work are more prone to take precautions or to "molly-coddle" their children.

Assessments by Health Visitors and School Teachers

While Douglas and Blomfield, in their national inquiry, were not able to find any overt evidence that the children of working mothers had more illnesses and accidents or suffered in their emotional development, fewer of the mothers working full-time showed the best ratings in all aspects of child care according to the health visitors. They were also less well-known to the health visitors and less frequently "very willing" to take their advice.

In discussions before our inquiry, health visitors and teachers working in the area expressed the almost unanimous opinion that working mothers were usually less conscientious and more apt to neglect their children. We asked the health visitors, therefore, to make certain judgements concerning the mothers of children under 5 who were included in our three-sixteenths sample. The teachers were asked to assess the co-operativeness of the parents of the children in the sample, and to state whether they considered the child well cared for or neglected.

Where health visitors were concerned, our results were similar to those of Douglas and Blomfield. The health visitors knew significantly fewer of the working mothers, and were consequently able to assess fewer. Of those working mothers whom they did know, they rated a relatively small proportion as providing "good" care of both the child's physical and emotional needs; but the numbers were small and no significance can be attached to the differences in assessment (Table XII).

TABLE XII

HEALTH VISITORS' ASSESSMENTS OF MOTHERS OF PRE-SCHOOL CHILDREN (PER CENT.), BY MOTHERS' EMPLOYMENT

Assessment of Mother				Working Full- and Part-time	Not Working
Care of Child	Physical and Nutritional Needs	Not Assessed ..		21	4
		Assessed	Good	18	26
			Average	82	67
			Poor	—	7
	Emotional Needs	Not Assessed ..		21	9
		Assessed	Good	18	21
			Average	56	68
			Poor	26	11
Personality or Intelligence Inadequacy ..				37	28
Sample (= 100 per cent.)				29	232

The teachers' assessments did not, on the whole, confirm their previously expressed opinions about mothers who worked (Table XIII).

TABLE XIII

TEACHERS' ASSESSMENTS OF PARENTAL ATTITUDES AND CARE (PER CENT.), BY MOTHERS' EMPLOYMENT

Teachers' Assessment		Mothers' Employment		
		Working		Not Working
		Full-time	Part-time	
Parents' Attitude to School	Particularly co-operative ..	18	26	17
	Reasonably co-operative ..	62	55	59
	Indifferent	18	18	23
	Hostile	2	1	1
	Sample (= 100 per cent.) ..	65	141	303
Care of Child	Particularly well cared for ..	44	45	35
	Adequately cared for ..	47	48	59
	Somewhat neglected ..	9	7	6
	Seriously neglected ..	—	—	—
	Sample (= 100 per cent.) ..	70	153	336

About one-fifth of the children were regarded as having parents who were indifferent or hostile to the school; but this proportion was not related to the mothers' employment. A rather high proportion of mothers who worked part-time was regarded as being particularly co-operative. Some of the part-time workers were employed in the schools as cleaners, canteen workers, or secretaries. It is possible, therefore, that higher assessments reflect greater familiarity.

None of the children in our sample was regarded by the teacher as being "seriously neglected", and less than one-tenth were described as "somewhat neglected"; but, as in the case of the parental attitude towards the school, this proportion was not significantly related to the mothers' employment. On the other hand, rather more of the children of working mothers than of those whose mothers did not work were regarded as being particularly well cared for, which may reflect the higher material standards of families in which the mother goes out to work.

Other assessments made by the teachers of the children's intellectual development and personality also fail to suggest a picture of the "neglected", "latch-key" child. For example, among primary school children, more of those with working mothers were regarded by their teachers as of higher than average intelligence, than of those whose mothers did not work (Table XIV).

TABLE XIV

TEACHERS' ASSESSMENTS OF INTELLIGENCE (PER CENT.), BY MOTHERS' EMPLOYMENT

Age Group of Children (yrs)		5–9		10 or More	
Mothers' Employment		Working	Not Working	Working	Not Working
Estimated Intelligence Quotient (per cent.)	120 orMore	5	5	7	2
	108–120	31	20	17	28
	92–108	39	34	42	44
	80–92	21	29	30	24
	Below 80	4	12	4	2
Sample (= 100 per cent.)		84	114	86	85

This difference was significant at the 5 per cent. level. There was no difference among the children of secondary school age who were assessed, but children attending grammar and technical schools were not included in these assessments.

In the primary school group, the reading ability of children of part-time workers was also rated more highly on the whole than that of those whose mothers did not work (Table XV).

TABLE XV

READING ABILITY OF CHILDREN AGED 6-9 IN JUNIOR SCHOOLS (PER CENT.), BY MOTHERS' EMPLOYMENT

Mothers' Employment		Working		Not Working (per cent.)
		Full-time (per cent.)	Part-time (per cent.)	
Reading Ability Percentile	A = Top 25 per cent.	21	36	25
	B = Middle 50 per cent.	58	44	48
	C = Bottom 25 per cent.	21	20	27
Sample (= 100 per cent.)		24	64	137

Besides assessing the children's intelligence and attainments in reading and some other subjects, the teachers were asked to place each child on a five-point scale for self-confidence, sociability, co-operativeness, perseverance, and conscientiousness. Very few children were placed at the extremes of the scale, and in our analysis the extremes were combined with their adjacent stages to make a three-point scale. The results for children aged 6–11 years in junior schools, grouped according to their mothers' employment, are given in Table XVI.

TABLE XVI

TEACHERS' ASSESSMENT OF CHILDREN'S CHARACTER (PER CENT.), BY MOTHERS' EMPLOYMENT

Mothers' Employment			Working		
			Full-time	Part-time	Not Working
Junior School Children Rated for	Self Confidence	Very self-confident	18	23	24
		Normally confident	49	51	44
		Timid or diffident	33	26	32
	Sociability	Very sociable	33	43	42
		Normally sociable	58	55	49
		Unsociable, solitary	9	2	9
	Co-operativeness	Very co-operative	33	44	30
		Normally co-operative	46	48	59
		Reluctant to co-operate	21	8	11
	Perseverance	Very persevering	27	27	25
		Normally persevering	36	49	51
		Lacking in perseverance	36	24	24
	Conscientiousness	Very conscientious	24	34	30
		Normally conscientious	46	52	53
		Careless, little pride in work	30	14	17
Sample (= 100 per cent.)			33	88	177

TABLE XVII

TEMPERAMENTAL CHARACTERISTICS REPORTED BY SCHOOL TEACHERS FOR CHILDREN WITH ROUTINE SCHOOL MEDICAL EXAMINATIONS (PER CENT.), BY MOTHERS' EMPLOYMENT

School		Junior		Secondary	
Mothers' Employment		Working	Not Working	Working	Not Working
Temperamental Characteristics	Nervous, tearful, apathetic, withdrawn, or over-dependent	17	21	16	20
	Exhibitionist, excitable, resentful of discipline, or spiteful	8	11	16	8
	None of above	81	72	76	74
Sample (= 100 per cent.)		48	136	58	78

These assessments show that the teachers, on the whole, found little difference in the self-confidence or sociability of children from the three groups. Where co-operativeness was at issue, the children of part-time workers seem to have excelled. The children of full-time workers, on the other hand, tended to be rated somewhat lower than other children in co-operativeness, perseverance, and conscientiousness.

Other assessments made by the teachers relate to children who had a routine medical examination during the spring term of 1957. No significant difference was found in the various temperamental characteristics enumerated in Table XVII between children whose mothers worked and those whose mothers did not work.

USE OF HEALTH SERVICES AND MOTHERS' EMPLOYMENT

Even if the health of children whose mothers work is similar to the health of children whose mothers do not work, it is possible that their use of the health services may differ. For example, Douglas and Blomfield found, in their sample of children under 5 years old, that hospital admissions were more frequent among the children whose mothers worked full-time than among those whose mothers worked part-time or not at all. They also found that the children of mothers working both full-time and part-time tended to stay longer in hospital once they had been admitted.

We found a similar difference between the admissions to hospital of children under 5 whose mothers worked and those of children whose mothers did not work; but our numbers were too small for us to say that such a result might not have occurred by chance. The smallness of our numbers also prevented us from comparing the lengths of stay in hospital of those whose mothers worked and those whose mothers did not work. Among children of school age, however, the difference in the proportions admitted to hospital is very small and without statistical significance when the two age groups are considered together. Among those aged 10 years and over, on the other hand, there was a higher proportion of children admitted to hospital in the previous year where the mother worked (Table XVIII).

TABLE XVIII

PERCENTAGE HOSPITAL ADMISSIONS IN 12 MONTHS BEFORE INQUIRY BY MOTHERS' EMPLOYMENT AND AGE OF CHILDREN

Age Group of Children (yrs)	Mothers' Employment	Percentage with Admissions to Hospital	No. of Children (= 100 per cent.)
Under 5	Working Full and Part-time	16	31
	Not Working	5	223
5–9	Working — Full-time	10	41
	Working — Part-time	13	106
	Not Working	12	246
10 and Over	Working — Full-time	7	55
	Working — Part-time	7	93
	Not Working	2	132

Variations in the use of the general practitioner's service—measured by the frequency of consultations—followed a different pattern. There was no statistically significant difference in the frequency with which mothers consulted the general practitioner about their pre-school children; but there was some indication that the children of school age whose mothers worked full-time were seen rather less frequently by the general practitioners than the children whose mothers worked part-time or not at all. Among children aged 5 to 9 years the difference was caused not so much by a larger proportion of children of full-time workers not being seen by the general practitioner at all, as by a small percentage seeing the doctor on five or more occasions. Among the children aged 10 years and over, on the other hand, a relatively high percentage of those whose mothers worked full-time had not consulted the doctor at all (Table XIX, overleaf).

TABLE XIX

FREQUENCY OF GENERAL PRACTITIONERS' CONSULTATIONS, BY MOTHERS' EMPLOYMENT AND AGE OF CHILDREN

Children registered with General Practitioners on Estate throughout 1953.

Age Group of Children (yrs)		Under 5		5–9			10 or more		
Mothers' Employment		Working	Not Working	Working		Not Working	Working		Not Working
		Full- or Part-time		Full-time	Part-time		Full-time	Part-time	
Percentage Children with Consultations (per year)	None	8	6	20	19	16	45	26	29
	One	8	15	20	12	19	13	14	21
	Two	29	12	17	16	14	9	24	18
	Three or Four	17	20	25	23	23	17	16	17
	Five to Seven	21 } 38	26 } 47	9 } 18	13 } 30	16 } 28	9 } 16	13 } 20	9 } 14
	Eight or More	17	21	9	17	12	7	7	5
Sample (= 100 per cent.)		24	135	35	84	193	46	76	103
Average No. of Consultations		4·2	4·8	2·6	3·9	3·4	1·9	2·6	2·2

We are not in a position to say why there should be a difference of this kind in the pattern of consulting by children of different ages whose mothers are working. A possible explanation is that the children aged 10 and over are more often expected to go to the doctor alone whereas the children less than 10 years old would be taken by the mother. This might lead to fewer of the older ones making any contact at all, whereas the mothers might be less inclined to pay repeated calls with the younger ones after an initial visit.

The teachers were strongly of the opinion that the School Minor Ailments Clinic on the estate was used excessively by children whose mothers were working as a substitute for the general practitioner. Our figures do not substantiate this impression; but the numbers involved were so small that it cannot be dismissed altogether. Interestingly enough, however, it was the children of part-time workers who seemed to use the school health services most frequently, and it was they who had the highest average consultation rates with the general practitioners (Table XX).

TABLE XX

PERCENTAGE OF CHILDREN USING SCHOOL HEALTH SERVICES DURING A 4-WEEK PERIOD, BY MOTHERS' EMPLOYMENT

Age Group of Children (yrs)	Mothers' Employment	Percentage of Children using School Health Service	No. of Children (= 100 per cent.)
5–9	Working — Full-time	5	40
	Working — Part-time	11	104
	Not Working	8	238
10 or More	Working — Full-time	6	52
	Working — Part-time	12	92
	Not Working	6	128

HEALTH OF MARRIED WOMEN WHO WORK

Hitherto we have been examining the evidence concerning the children of mothers who work. We now turn to a consideration of the health of the women themselves. We have already shown that women's employment is closely related to age, to the number of children, and to the age of the youngest child. These factors are also likely to affect women's health, their use of the health services, and their need and ability to stay in bed when unwell. We cannot, therefore, consider how far the married women who work differ in health, in the use of services, and in the extent to which they are "incapacitated", from married women who are not gainfully employed if we do not take into account the association of these factors with age and family size.

In this complex situation a much larger study than ours would be needed to allow us to assess the statistical significance of the relationship which we found between the employment of married women and the extent to which the general practitioner was consulted. We found, for example, that married women under 45 who worked had a higher average annual consultation rate than those who did not work (Table XXI).

TABLE XXI

AVERAGE ANNUAL NUMBER OF G.P. CONSULTATIONS FOR MARRIED WOMEN UNDER AGE 45, BY EMPLOYMENT AND BY NUMBER OF CHILDREN

Married Women under Age 45		Average Annual No. of General Practitioner Consultations	No. in Sample*
Employment	Working — Full-time	5·3	62
	Working — Part-time	4·9	77
	Not Working	4·1	203
No. of Children	0	6·1	19
	1	5·1	58
	2	4·1	120
	3	4·7	89
	4 or More	3·7	54

* Only those registered with the General Practitioners on the estate throughout 1954 have been included.

At the same time, the more children a married woman had, the lower was her consultation rate. It is possible, therefore, that the higher consultation rate of employed women was no more than a reflection of their other attribute—fewer children. Alternatively, the higher consultation rate of women with no children or only one child might reflect the fact that they were more likely to be gainfully employed.

A cross-analysis (Table XXII) appears to indicate that, in practice, both employment and size of family influenced the general practitioner consultation rate. On the one hand, among women under 45 with a similar number of children, those in paid employment visited their general practitioner more frequently than those not gainfully employed. On the other hand, among workers and non-workers alike, those with fewer children had a higher consultation rate than those with more children.

TABLE XXII

AVERAGE NUMBER OF GENERAL PRACTITIONER CONSULTATIONS OF MARRIED WOMEN UNDER AGE 45, BY EMPLOYMENT AND BY NUMBER OF CHILDREN

Married Women's Employment	Working				Not Working	
	Full-time		Part-time			
Number of Children	Average Annual G.P. Consultation Rate	No. in Sample	Average Annual G.P. Consultation Rate	No. in Sample	Average Annual G.P. Consultation Rate	No. in Sample
0 or 1	6·7	17	5·2	19	4·7	40
2	4·8	25	4·6	28	3·6	66
3 or More	4·8	18	4·9	29	4·1	94

If, however, we were to try to take into account, in addition to numbers of children, the age of the youngest child, which we know to be associated with employment, the resulting numbers would be so small as to make the analysis valueless.

It is platitudinous to point out that there is not a direct relationship between frequency of consultation with a general practitioner and actual illness. Many subjective factors will influence the way in which individuals use the service, among the most important of which is likely to be individual differences in the toleration of pain and discomfort. Moreover, social factors, not in themselves related to the illness, will also influence consultation rates. For example, in a society where employers and state demand that sickness absence shall be certified by a doctor, differences in the frequency with which individuals consult may be primarily related to their need to obtain certificates. Some such factor may be responsible for the observed differences between workers and non-workers in our sample. Again, it is probable that mothers of large families and those with several dependent children find it more difficult to spare the time to visit the doctor than women who have few children or none. This may explain the differences in the consultation rate with differing numbers of children.

DAYS IN BED

Similar considerations are likely to affect the frequency with which women stay in bed. There are difficulties in deciding what shall be called "a day in bed". For example, part of an invalid's day may be spent sitting in a wheeled chair, or household duties may force a housewife to get up from time to time. However, when we asked the women in our sample whether they "had stayed in bed for any days or half-days" during the 4-weeks between our two interviews, a higher proportion of those who were working than of those who were not working, and more of those who were working full-time than of those who were working part-time said "yes"*. When they were asked whether there was any occasion upon which they would have liked to stay in bed, however, the position was reversed (Table XXIII). It would seem, therefore, that among our sample of married women there was little difference between the working and non-working women in their assessment of their need to stay in bed. They differed primarily in their capacity to do so.

TABLE XXIII

PERCENTAGE OF MARRIED WOMEN UNDER 45 WITH DAYS IN BED (ACTUAL AND DESIRED), BY EMPLOYMENT AND BY NUMBER OF CHILDREN

Days in Bed		One or More Days in Bed during 4-week Period	Would have liked to stay in Bed if Possible	Sample (= 100 per cent.)
Married Women's Employment	Working Full-time	13	18	85
	Working Part-time	6	23	94
	Not Working ..	4	30	267
No. of Children	0	16	9	32
	1	7	32	82
	2	7	23	142
	3	8	31	114
	4 or More	1	29	72

These differences, like those in general practitioner consultations, were also shown to reflect to some extent the different family responsibilities of working and non-working women. The percentage of women with no children who stayed in bed was almost

* Numbers were too small to make comparisons by the number of days in bed.

double the percentage of those who would have liked to have stayed in bed if they could; whereas, among women with children and particularly among those with four children or more, the percentage who actually took to their beds was only a small fraction of those who would have liked to have done so.

We have already suggested that the observed differences between working and non-working women in frequency of general practitioner consultations or of days in bed can be a function of their social obligations—including family size—rather than a reflection of their real experience of illness. The answer to the questions put to all the women interviewed concerning their health at the time tend to confirm the impression that there is little discernible difference between the general level of health—if it is permissible to talk in this way—of working mothers and that of non-working mothers. For example, there was no significant difference in the number of illnesses reported by women grouped by age and employment experience (Table XXIV).

One or two differences do, however, emerge when we consider the proportion of married women reporting particular symptomatic conditions about which they were asked specifically. For example, constipation was reported more frequently by working women, particularly by those aged 45 to 54. In this latter age group, indigestion and "nerves" were also alleged much more frequently by the workers. On the other hand, "undue tiredness" was reported less frequently by the workers than by the non-workers (Table XXV).

These were the largest and most consistent differences between working and non-working women. Other differences were too small to warrant conclusions or were inconsistent, in the sense that the relative size of the proportions in different age groups were reversed, the workers in one age group and the non-workers in another being more prone to illness. All in all, therefore, we felt it legitimate to

TABLE XXIV

AVERAGE NUMBER OF ILLNESSES REPORTED BY MARRIED WOMEN UNDER 55, BY EMPLOYMENT AND AGE

Woman's Age (yrs)		Under 35		35–44		45–54		All Under 55	
		Average No. of Illnesses	No. in Sample	Average No. of Illnesses	No. in Sample	Average No. of Illnesses	No. in Sample	Average No. of Illnesses	No. in Sample
Married Women's Employment	Working: Full-time	3·3	39	3·5	46	3·6	36	3·4	97
	Working: Part-time	3·6	35	3·2	59			3·4	118
	Not Working	3·0	158	3·4	109	3·6	42	3·2	309
	All Groups	3·2	232	3·3	214	3·6	78		524

TABLE XXV

PERCENTAGE OF MARRIED WOMEN REPORTING VARIOUS CONDITIONS, BY EMPLOYMENT AND AGE

Woman's Age (yrs)		Under 35			35–44			45–54	
Employment		Working		Not Working	Working		Not Working	Working	Not Working
		Full-time	Part-time		Full-time	Part-time		Full- or Part-time	
Condition Reported (per cent.)	Backache	28	34	21	33	31	41	33	48
	Breathlessness	18	20	16	13	24	32	25	38
	Catarrh	21	40	30	22	31	28	31	19
	Colds	23	37	22	17	20	21	22	17
	Constipation	21	23	15	26	10	10	17	—
	Coughing	10	23	18	22	15	19	14	7
	Depression	18	20	21	28	27	28	31	31
	Dizziness	5	9	12	9	14	21	14	21
	Eye Strain	23	17	22	17	15	16	30	36
	Headaches	41	40	38	39	42	43	39	33
	Indigestion	15	14	13	22	15	19	33	5
	Nerves	28	34	27	37	32	35	42	19
	Painful or Swollen Joints	18	17	6	24	20	26	25	24
	Palpitations	15	9	13	9	14	23	22	24
	Rheumatism	28	26	15	20	34	29	36	40
	Sleeplessness	5	9	14	24	7	11	28	36
	Swollen ankles	21	11	9	26	19	20	25	33
	Trouble with Teeth	8	14	18	7	12	19	11	5
	Undue Irritability	5	11	18	9	8	18	14	14
	Undue Tiredness	—	20	20	13	12	20	11	26
	Varicose Veins	13	17	22	24	20	20	17	26
	Weak or Painful Feet	10	—	10	17	24	13	25	12
	Women's Complaints	18	43	27	26	31	35	44	29
Total Women (= 100 per cent.)		39	35	158	46	59	109	36	42

conclude that differences in health are unlikely to lie behind the difference in general practitioner consultations rate or in days in bed between working and non-working married women.

Summary

Information about the employment of married women living on an estate just outside London is related to various indices of their own and their children's health, incapacity, and use of the health services, as well as to their own ages and to the size, age, and composition of their families. Very few women with children under 2 years old went out to work, but about half of those whose youngest child was of school age did so. Little difference was observed in the reported health of the women who worked and that of those who did not; but those who did work tended to see their general practitioner rather more frequently and appeared to be better able to spend a day or two in bed if they felt like it than women who were not "gainfully employed".

The proportion of children whose mothers worked increased with the age of the child, the child's position in the family being also an important factor. The youngest member of the family was more likely to have a mother who worked than older members of the family had been at the same age. No excess of illness among children with working mothers was found; nor were there any overt signs that these children were affected emotionally. They had fewer absences from school than children whose mothers did not work, and, among children of school age, there was some indication that children whose mothers worked full-time were seen rather less frequently by the general practitioners than children whose mothers worked part-time or not at all. Among children under school age our figures are consistent with those of Douglas and Blomfield, who found that hospital admissions were relatively frequent among those whose mothers worked full-time.

In general discussions both health visitors and school teachers on the estate had spontaneously and almost unanimously expressed some criticisms of working mothers and their care of their children; but when they were asked to rate individual parents on certain scales there was no statistically significant evidence to show that families in which the mothers went out to work were particularly unsatisfactory. Other assessments by school teachers showed that, among primary school children, those with working mothers were considered to be rather more intelligent and their reading ability greater than that of other children.

We concluded that on this estate, with the existing pattern of employment among married women, there was no evidence to suggest that children whose mothers went out to work were relatively neglected or handicapped either physically, intellectually, or emotionally.

The programme of research of which this study formed a part was directed by Professor J. H. F. Brotherston, formerly Reader in Public Health at the London School of Hygiene and Tropical Medicine. We should like to thank him and Professor W. S. Walton for invaluable advice and criticism. We are also grateful to Mr. S. P. W. Chave, Miss M.W. Grant, and other colleagues in London and Edinburgh for data and assistance, to Dr. F Barasi of the Hertfordshire County Council, to the health visitors, teachers, and officials in the area, and to the interviewers and office staff, all of whom worked with us and made this study possible.

REFERENCES

Brotherston, J. H. F., Chave, S. P. W., and six others (1956). *Brit J prev. soc. Med.*, **10**, 200.

Douglas, J. W. B., and Blomfield, J. M. (1958). "Children under Five" Allen and Unwin, London.

Brit. J. prev. soc. Med. (1958), **12**, 172–182

SICKNESS, CHANGE OF RESIDENCE, AND DEATH*

I. GENERAL RESULTS OF FOLLOW-UP IN TWO POPULATION GROUPS

BY

DONOVAN J. THOMPSON AND ANTONIO CIOCCO

Department of Biostatistics, Graduate School of Public Health, University of Pittsburgh

INTRODUCTION

In this paper we present some basic data on residence changes and mortality experience observed in a population sample of (*a*) the Arsenal Health District of Pittsburgh, Pa, from 1951 to 1956; and (*b*) Donora, Pa, from 1948 to 1957.

The analyses of these data seek to answer only two questions at this time:

(1) Are the movement (*i.e.* change of residence) and mortality experiences of persons who complain of some sickness in a household interview survey different from the experiences of those who have no such complaint?

(2) To what extent are the estimates of mortality rates affected by the loss of a portion of the originally designated sample through change of address?

Both questions bear upon the increasing efforts being made to describe the natural history of the diseases which now predominate as causes of disability and death, and to identify the significant time periods in which to search for possible aetiological factors of these conditions.

For these purposes studies are needed which can cover a considerable span of time before the onset of disability or death from the chronic diseases. Data obtained through household sickness surveys, of which many have been made in recent decades (Logan and Brooke, 1957), can provide a starting point for such long-term studies, as we hope to show in this and following papers. This point was illustrated in the resurvey of the Hagerstown population after 20 years (Ciocco, 1946; Lawrence, 1948), which led to the conclusion that "A substantial proportion of the persons who are ill at 65 have had the same or another chronic illness for at least 20 years" (Ciocco and Lawrence, 1952). However, as has been learned from these and many other studies which seek to relate certain individual characteristics at one point in time to the development of disease conditions later, a number of problems of analysis and interpretation arise. These problems are due in part to the bias resulting from the selection of the population under observation (Berkson, 1955), to effects of the passage of time on the development of the condition under study (Kodlin and Thompson, 1958), to the non-specific nature of the characteristic chosen for the initial observation, or to poor definition of the onset of the conditions under study.

In brief, while it is well recognized that long-term studies are required to elucidate the factors related to the onset of the numerically important disabling and fatal diseases of current preoccupation, more knowledge is required to provide a sound basis for carrying out such studies. Moreover, the tools for the analyses of these studies are still somewhat crude, so that the findings resulting from them cannot be readily interpreted. There is a definite need, therefore, to explore and probe further into the statistical as well as into the observational methodology of long-term investigation of chronic disease. The study here reported with others planned in this series constitutes an example of such exploration.

* This work was supported in part by a research contract with the Air Pollution Medical Program, Public Health Service, U.S. Department of Health, Education, and Welfare.

MATERIAL AND METHOD

SOURCE.—The two population groups under study are:

(1) *A sample of the population in a section of the Arsenal Health District of Pittsburgh.*—From this section which, according to the 1950 census, had a population of 81,785 persons, an equal probability sample of 2,954 dwelling units was selected for a household interview survey during July, 1951 (Horvitz, 1952). The survey aimed at obtaining data on such demographic characteristics as age, sex, marital status, nativity, education, etc; on illnesses which had occurred in the month before the survey and services of physicians, hospitals, and clinics received during this period; on hospitalizations and accidents or injuries requiring hospitalization or physician services during the year preceding the survey. Completed interviews were actually obtained from 2,791 households including 9,749 persons, of whom 6,305 were 21 years of age and over in 1951. It is this number that constitutes the base population group followed to July, 1956.

(2) *A systematic one-third sample of the households of Donora, Pa, listed in the* 1947 *files of the Tax Assessor of the Borough.*—This survey was conducted in 1948 by the U.S. Public Health Service (Schrenk, Heiman, Clayton, Gafaver, and Wexler, 1949). Data were obtained from a responsible person in the household on all members of the household with regard to:

(*a*) such demographic characteristics as age, sex, marital status, occupation, residence;

(*b*) past experience of specific conditions such as asthma, sinusitis, heart disease, chronic bronchitis, tuberculosis;

(*c*) the occurrence of symptoms such as cough, nausea, vomiting, headache, and smarting of the eyes during the smog episode of late October, 1948;

(*d*) the persistence of these symptoms,

(*e*) physician and hospital services obtained for the ailments.

Information was obtained by this survey on 4,092 residents of Donora, of whom 2,712 were 21 years of age and over at the time of the survey and constitute that part of the population group followed to 1957 which will be discussed here.

The two population groups differ in many respects as has been indicated and can be surmised; the objectives of the two surveys differed, as did the approach to the selected households and the techniques of obtaining information on illness. Finally, the follow-up mechanism and information was quite different for the two groups.

FOLLOW-UP PROCEDURES.—For the Arsenal sample, subsequent information on change in residence results from a combination of several procedures:

(1) In July, 1952, one year after the original survey, the total sample of households was resurveyed by the same household interview method; and information of the same kind as in the first survey, but more extensive for selected chronic diseases, was obtained. The second survey thus provided data on the number of persons who had moved or died in the year's interval. No attempt was made to trace the persons who had moved. It should be noted also that at the second survey, the interviewers were unaware of the status or other characteristics of the households interviewed at the first survey.

(2) In July, 1956, in connexion with other investigations, the National Cancer Institute requested the Post Office Department for information on changes of address of the whole group of 6,305 persons. The information obtained and made available to us indicated for each individual whether he resided in July, 1956, at the address of 1951, had moved from that address, or was known to have died while residing at that address.

(3) A listing of all deaths of residents of Allegheny County from July, 1951, to July, 1956, was made available to us by the Department of Vital Statistics of the Commonwealth of Pennsylvania. The names of all the 6,305 persons were checked against this listing.

Procedure (3) has provided the basic information on mortality for this study. It revealed, as was to be expected, that the Post Office inquiry missed some of the deaths (approximately one-third) listed in the Vital Statistics Office. Procedure (2) has provided the basic information on the number of persons residing in 1956 at the address of 1951.

As a result of the procedures employed, it can be assumed that we possess fairly reliable information on the identity of the persons who in July, 1956, resided at the 1951 address, and of the persons who died within Allegheny County during the interval 1951–1956. No information is available on the dates of change of residence after 1952 or on the deaths which occurred outside Allegheny County. Supplementary data were obtained through special studies conducted on segments of this population for other purposes. Sub-samples were selected for studies on the prevalence of arthritis (Cobb, Thompson, Rosenbaum, Warren, and Merchant, 1956) and on the prevalence of heart disease (Tauber and Thompson, 1957). The survivors of the arthritis

study group, which to begin with involved 944 persons, are still under periodic observation. The heart study group involved, to start with, 778 persons, who were kept under observation until the middle of 1954. Even with these supplementary data it is anticipated that the identification of deaths and movement is subject to some errors. Specifically, we believe that deaths and movements may be underestimated.

The follow-up procedures in Donora were direct, thus avoiding some of the "errors" inherent in the Arsenal material. These procedures consisted of the following steps:

(1) A complete census of all the households of the Borough of Donora was made in February-March, 1957.

(2) If no member of the household sampled in 1948 remained at the original address, information was sought from the neighbours or current residents as to the present whereabouts of the listed individuals of that household, and, in addition, a central file was established so that information became immediately available if members of that household has been contacted in some other part of the borough.

(3) Letters were sent to every person who had left Donora. As a result, contact was made with that person or with other members of his household in the case of 99·1 per cent. of the persons listed in the original survey.

In the Donora follow-up, information was obtained on the incidence and prevalence of certain chronic conditions during the interval 1948–1957 as well as on hospitalization and medical services received in the interval, place and cause of death, etc. It should be emphasized that the 1957 interviewers were not aware of the responses to health questions which had been made in 1948. Findings related to these aspects of the Donora follow-up will be presented in other publications.

Definitions.—In the 1951 survey of the Arsenal Health District, the respondent was asked questions such as: "Has anyone in the household been ill in bed, been ill at home, or called in or visited a physician during the past month? Has anyone been injured or involved in an accident for which medical care was sought during the past year?"

If the answer to any of these questions was "yes" the person involved was classified as "ill", unless the reason given for the answer indicated that the episode concerned normal pregnancy or childbirth, routine physical examinations, immunizations, etc.

In the 1948 survey of Donora, the main question was: "Were you affected by the smog of October 28–31?"

If the answer was "yes", the persons involved were placed in the class: "acute illness". Inquiry was also made regarding the prevalence of certain chronic illnesses such as asthma, heart disease, chronic bronchitis, tuberculosis, and sinusitis. Persons with these conditions and/or acute illness are included in the "all illness" class.

One other difference in the study of the two samples is in the definition of movement. For the Arsenal sample, information is available primarily on whether or not the subject was living in 1956 at the 1951 address. More complete information was obtained on the Donora sample. For the purpose of this study, the term "movement" for the Arsenal sample means change in first address, for the Donora sample it means leaving the borough.

Description of Movement or Death

In 1956, information was obtained that 368 of the 6,305 persons in the Arsenal sample had died between 1951 and 1956 and that 2,347 had moved from the 1951 address. For all but fourteen of the deaths, copies or abstracts of the death certificates are at hand. For the Donora sample, the resurvey of 1957 found that 298 of the 2,712 had died and that 456 had left Donora in the 8½ years that had elapsed between the two surveys. Copies or abstracts of the death certificates are available on 276 of the dead.

The findings on movement and death are summarized by sex, by broad age groups, and by illness experience reported at the initial survey in Tables 1A and 1B.

The major points to note are:

(1) The expected difference between the two sexes with respect to mortality is evident, but there is little sex difference with respect to movement.

(2) The percentage of known deaths increase with increase in age at first observation, but the percentages of persons who moved decrease with age.

(3) In the Donora sample (Table 1A), for each sex and for each age group, the percentage of ill persons who had died in the 8½-year interval is larger than the percentage of persons who died during the 8½-year interval but were not reported ill during

TABLE IA

DONORA SAMPLE, STATUS IN 1957 ACCORDING TO ILLNESS EXPERIENCE REPORTED IN 1948

Age (yrs)	Males						Females			
	In 1948		Percentage in 1957				In 1948	Percentage in 1957		
	Illness* Reported	Number	In Donora	Left Donora	Dead		Number	In Donora	Left Donora	Dead
21–34	None	238	72·6	26·6	·8		252	69·3	29·9	·8
	Acute Only	157	64·3	32·5	3·2		203	73·9	24·6	1·5
	All	187	64·9	32·4	2·7		240	73·9	24·9	1·2
35–49	None	166	83·7	13·3	3·0		162	85·8	11·7	2·5
	Acute Only	222	82·4	12·2	5·4		199	81·4	12·1	6·5
	All	243	82·3	12·3	5·3		232	81·0	12·5	6·5
50–64	None	136	69·9	14·7	15·4		128	82·8	6·3	10·9
	Acute Only	235	72·3	8·9	18·7		174	72·4	10·9	16·7
	All	266	70·7	9·0	20·3		193	72·0	10·4	17·6
65 and Over	None	44	50·0	4·5	45·5		43	55·8	2·3	41·9
	Acute Only	82	42·7	7·3	50·0		69	40·6	15·9	43·5
	All	100	40·0	9·0	51·0		82	39·0	15·9	45·1

* The "all" illness category includes the "acute only" plus persons reporting only chronic illness.

TABLE IB

ARSENAL SAMPLE, STATUS IN 1956 ACCORDING TO ILLNESS EXPERIENCE REPORTED IN 1951

Age (yrs)	Males						Females			
	In 1951		Percentage in 1956				In 1951	Percentage in 1956		
	Illness Reported	Number	At same Address	Changed Address	Dead		Number	At same Address	Changed Address	Dead
21–34	No	846	44·9	53·8	1·3		901	47·3	52·7	—
	Yes	96	54·1	43·8	2·1		161	43·5	54·7	1·9
35–49	No	862	64·1	33·9	2·0		871	66·5	32·4	1·1
	Yes	133	51·9	43·6	4·5		213	57·3	36·6	6·1
50–64	No	597	65·5	25·1	9·4		559	65·5	29·0	5·5
	Yes	133	54·1	24·8	21·1		187	63·6	28·9	7·5
65 and Over	No	247	51·8	25·1	23·1		261	56·7	22·6	20·7
	Yes	100	43·0	18·0	39·0		138	52·1	28·3	19·6

the smog episode. The differences between the percentages do not increase or decrease consistently from the younger to the older age groups; however, there is a tendency for the ratios of the corresponding percentages to decrease from the younger to the older age groups.

(4) The percentage of ill persons who left Donora in the $8\frac{1}{2}$-year interval is higher than the corresponding percentage among persons not reported ill who left Donora in two of the four age groups among males and three of the four age groups among females. Thus it would appear that there is no consistent difference between the ill persons and the persons not reported ill with respect to migration from Donora.

(5) In the Arsenal sample (Table IB) for each sex and for each age group (except females 65 years of age and over) the percentage of persons who died during the interval 1951–1956 is higher among the persons reported ill in the 1951 survey than among those not reported ill. This difference is more striking in the males than in the females.

(6) Among the females in three of the four age groups in the Arsenal sample, the percentage of persons who moved is higher for those who reported illness in the 1951 survey than those who did not. Among the males this is observed in only one age group.

Before proceeding to an estimate of the mortality rates, let us consider the above findings. Taken at face value they indicate that reported illness, be it the acute variety associated with a smog episode or a conglomeration of acute and chronic conditions as found in the Arsenal survey, segregates from the population a group which for a few years at least will have a higher mortality than the rest. Further

analyses of our data will seek to determine the circumstances in which the differences persist. Some illnesses or conditions are undoubtedly more important than others in such segregation. From the data of the Hagerstown resurvey which took place after an interval of 20 years, the conclusion was reached that the life span was shortened only when major chronic conditions were reported in the initial survey. Future examination of the material at hand on the Arsenal and Donora samples will indicate how valid such conclusion is for the shorter span of time involved here. The lack of striking differences in mortality between the ill and not-ill females in the oldest age group of the Arsenal sample also deserves additional examination, since it may reflect the respondent bias often suspected in household surveys.

In a subsequent paper it will be shown that the differences in movement rates between the ill and not-ill persons probably reflect only sampling variation. Nevertheless, the amount of the change is considerable, and is an important factor to consider in any attempt at follow-up of population samples. It creates an important problem for the estimation of mortality rates as we shall next point out.

Estimation of Mortality Rates

The data we have described relate mortality and mobility through time in two groups of persons—the "ill" and the "not ill". In many follow-up investigations, the persons we have described as "moved" would be lost to follow-up on the date of their first movement. In some investigations diligent efforts are made to keep this moved group under observation, but nevertheless some fraction (large or small) is finally lost to follow-up. The careful investigator is concerned with the possible influences such losses may have in contrasting two or more groups, such as our "ill" and "not ill", in terms of mortality or any other characteristic. From this point of view the movement experience can be viewed as a disturbance the possible influence of which requires investigation. The principal fear appears to be that the remnants remaining under observation at the end of some time period will not be "representative" of their respective initial groups. Differential selection of the "movers" in the various groups is, perhaps, viewed as the principal mechanism responsible for any lack of comparability among the remnants of each group at the end of some time period.

In this material, the data for the Donora sample include information about the date of movement from the borough of all the persons who moved, and about the date and place of death of those who died during the interval 1948 to 1957. For the Arsenal sample, in the interval 1952–56, information is available only about the date and place of death of those who died and could be found in the vital statistics records, but no information was obtained about the date of change of residence within the period. Since the Donora data are more complete, the analytical procedures to be described will be based on these data to begin with.

The events of death and movement in a series of discrete intervals of time may be shown graphically as in the Figure (opposite). During the first interval, (t_0, t_1), the persons in the cohort have a probability of dying, P_1, and a probability of moving, R_1. By the end of the first period, t_1, the persons alive at the beginning time point, t_0, will be found in one of the four categories indicated by the four following cells:

Category	*Probability*
Moved and Died	ϕ_{12} (1)
Moved and Survived	ϕ_2 (1)
Not moved and Died	ϕ_1 (1)
Not moved and Survived	ϕ_0 (1)

In the next interval, t_1 to t_2, we have two categories of living persons to consider (indicated by the broken arrows): those who moved and those who did not move during the first period. If we are not interested in the subsequent movement of those who moved in the interval t_0 to t_1, we can consider that during the interval t_1 to t_2 they are subject only to the risk of dying, the probability of which is designated as $P_2^{(1)}$. The survivors of the first period who did not move are again subject to both movement and death during the interval t_1 to t_2, and their probability of dying in the interval is designated as P_2, which may be the same as $P_2^{(1)}$ or may have a different value. The survivors at t_2 are of three types, as may be noted from the Figure, and for the period t_2 to t_3 a probability of dying is defined for each of the three types, P_3, $P_3^{(2)}$, $P_3^{(1)}$, which may again be identical or different.

In terms of this representation of the events of movement and death and their associated probabilities, the total probability of dying during the interval t_1 to t_w, designated P_t, is given by:

$$P_t = \left[\prod_{i=1}^{w-1}(1-P_i)\right]^{-1} \sum_{j=1}^{w}\left\{\prod_{i=0}^{j-1}\phi_0(i)\phi_2(j)\prod_{i=j+1}^{w-1}(1-P_i)\left[1-\prod_{i=1}^{j}(1-P_i)\prod_{i=j+1}^{w}(1-P_i^{(j)})\right]\right\}.$$

The observed frequency of occurrence of the various categories of events in the model will furnish the basic information for estimating the probabilities defined. For the case of complete follow-up for the period t_0 to t_w, P_t would be estimated simply by dividing the total observed deaths (ignoring movement) by the number of persons in the original sample.

If the follow-up of the movers is incomplete, as is most frequently the case, we may be forced to base our calculations of mortality rates on the incomplete experience obtained by following each individual to the end of the period during which he moves. From the model described in the Figure we shall then be estimating a total probability of dying during the interval t_0 to t_w defined as P_s, where

$$P_s = 1 - \prod_{i=1}^{w} (1 - P_i).$$

If the subsequent mortality of the "movers" and of those not moving is identical, $P_t^{(j)} = P_t$ for all $j < i$; $i = 2, \ldots, w$; P_s and P_t are identical. However, if the subsequent mortality of the movers and those not moving is different, P_s may differ from P_t.

If we limit our consideration of mortality only to those who moved at some time during the period of follow-up, we can calculate a total probability of dying for those who moved, P_m, in the following fashion:

$$P_m = \frac{d_m}{m},$$

where m is the total number moved, and d_m is the number of deaths occurring from the moved group.

As defined, P_m is a measure of the composite mortality at a stated point in all the subgroups that have moved before that point. It may easily be shown that P_m is a simple weighted average of the total probability of dying before the stated point in each of the subgroups. The weights used in the averaging process are the probabilities that a study person will be included in a particular subgroup. If $P_t^{(i)}$ has the same definition for the subsequent mortality in the subgroup which moves during the ith period as P_t has for the total study group, and if the relative weights are denoted by α_i,

$$P_m = \Sigma\, \alpha_i\, P_t^{(i)}.$$

The probabilities P_m, P_s, and P_t are, in general, related in the following way:

$$P_t - P_s = k\left\{P_m - P_m^*\right\}.$$

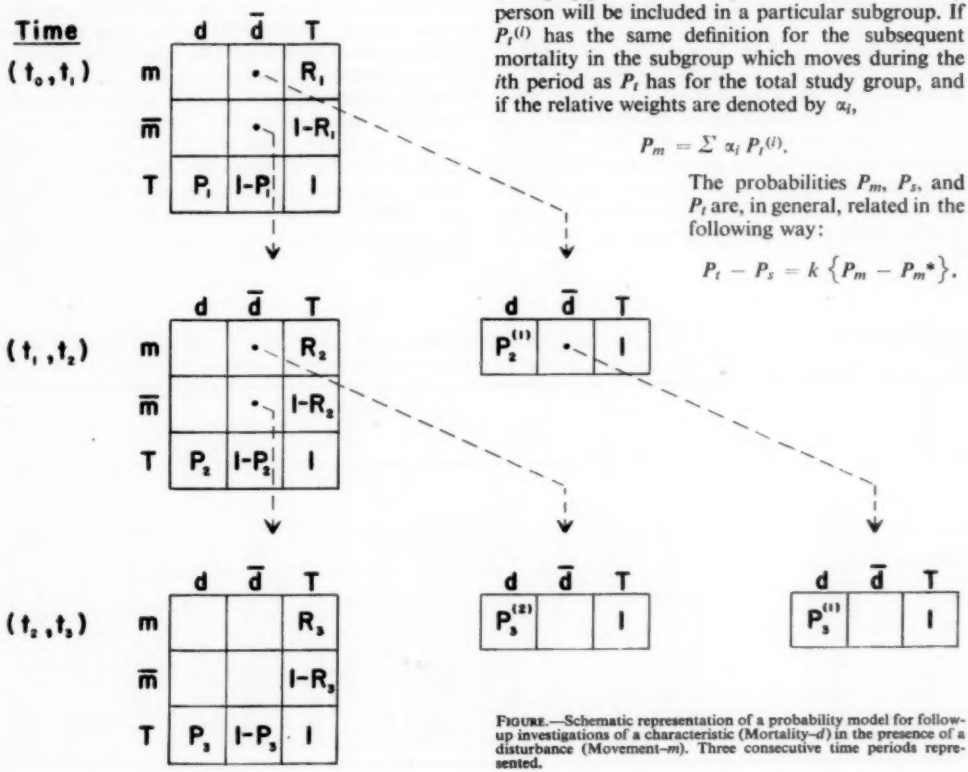


FIGURE.—Schematic representation of a probability model for follow-up investigations of a characteristic (Mortality–d) in the presence of a disturbance (Movement–m). Three consecutive time periods represented.

In this equation, k is a proportionality constant and P_m^* has the same functional form as P_m, with $P_i^{(j)}$ replaced by P_i throughout.

Further to clarify the interpretation of P_m, we might calculate the survivors to say, 1953, of the sub-group which moved in 1948 and survived that period, and the survivors of the subgroups which moved in the years 1949–1952. The total number of persons in these subgroups multiplied by $(1 - P_m)$ will give the total survivors to 1953 of these subgroups. It can also be shown that this calculation yields the same result as would be obtained by employing the usual actuarial or life-table methods appropriate for open cohorts.

For the Donora data, the probabilities so calculated are shown in Table II, which shows:

(1) The probability of dying (expressed by P_t) is greater among the ill than among the not ill for all ages and both sexes. However, the differences for corresponding intervals is not constant but increases to about 1948–53 and decreases thereafter.

(2) In the younger age group, the probability of dying for those who moved (as expressed by P_m) is zero, but in the older age group it is, for some intervals, slightly higher than the total probability (P_t) or the probability of dying while in Donora (P_s). The numbers involved during the intervals when this is observed are too small to give reliable rates. For the same reason not too much weight can be given to the higher values of P_m in the comparison of the ill and the not ill.

It must be recalled that the entrance into the moved group of a subgroup with subsequent low mortality will produce a decrease in the value P_m at that point, as is seen in Table II for ages 50 and over for the cumulative periods 1948–53.

(3) In the younger age group, the values of P_s are uniformly equal to or greater than the corresponding values of P_t. In the older age group, the influence of mortality among those who moved is reflected in the fact that for some intervals P_s may be smaller than P_t. For the whole period 1948–1957, P_s is greater than P_t for both age groups and both sexes.

(4) The relative differences, $(P_s - P_t)/P_t$, range from zero to as much as 18 per cent., the numerically larger relative differences being associated in general with periods for which the rates are low.

These findings bring out two important points for consideration. First, that the influence of the factor of the one episode of illness on subsequent mortality would become undetectable in the long run if the apparent trend continued. One may conclude from from this that, in long-term studies in which the relationship is sought between the manifestation of a condition and subsequent mortality or other measure of health, there will be an optimal period in which it is possible to measure the influence of the factor. Secondly, the mortality rates among those who moved and those who stayed are different. This strengthens the idea that a certain risk is involved in determining mortality rates on the assumption that

TABLE II

CUMULATIVE PROBABILITY OF DYING BETWEEN 1948 AND SUBSEQUENT YEARS IN DONORA SAMPLE, ACCORDING TO SEX, AGE, AND ILLNESS STATUS IN 1948, AND MOVEMENT STATUS IN SUBSEQUENT YEARS

Sex	Time Interval	Age (yrs)											
		21–49						50 and Over					
		Acute Illness in 1948			No Illness in 1948			Acute Illness in 1948			No Illness in 1948		
		P_t	P_s	P_m	P_t	P_s	P_m	P_t	P_s	P_m	P_t	P_s	P_m
Male	1948–49	0·005	0·005	—	0·002	0·002	—	0·022	0·022	—	0·022	0·022	—
	1948–50	0·011	0·011	0·0	0·002	0·002	0·0	0·057	0·057	0·0	0·039	0·039	0·0
	1948–51	0·018	0·019	0·0	0·007	0·008	0·0	0·114	0·116	0·0	0·061	0·051	0·286
	1948–52	0·021	0·022	0·0	0·007	0·008	0·0	0·142	0·145	0·0	0·100	0·091	0·286
	1948–53	0·021	0·022	0·0	0·012	0·013	0·0	0·180	0·187	0·0	0·128	0·121	0·182
	1948–54	0·032	0·035	0·0	0·012	0·013	0·0	0·199	0·208	0·053	0·156	0·151	0·154
	1948–55	0·034	0·038	0·0	0·017	0·019	0·0	0·246	0·255	0·053	0·189	0·188	0·125
	1948–57	0·045	0·051	0·0	0·017	0·019	0·0	0·268	0·279	0·045	0·228	0·233	0·095
Female	1948–49	0·002	0·002	—	0·002	0·002	—	0·021	0·021	—	0·012	0·012	—
	1948–50	0·015	0·015	0·0	0·002	0·002	0·0	0·058	0·058	0·0	0·018	0·018	0·0
	1948–51	0·022	0·023	0·0	0·002	0·002	0·0	0·078	0·079	0·0	0·035	0·035	0·0
	1948–52	0·022	0·023	0·0	0·005	0·005	0·0	0·111	0·113	0·0	0·053	0·053	0·0
	1948–53	0·025	0·026	0·0	0·005	0·005	0·0	0·144	0·148	0·0	0·082	0·078	0·250
	1948–54	0·032	0·035	0·0	0·005	0·005	0·0	0·189	0·197	0·0	0·117	0·114	0·167
	1948–55	0·032	0·035	0·0	0·012	0·014	0·0	0·222	0·228	0·056	0·152	0·151	0·167
	1948–57	0·040	0·044	0·0	0·014	0·017	0·0	0·243	0·247	0·091	0·187	0·188	0·111

there is equality in the mortality rates of those who moved and those who did not.

The P_t as calculated is a measure of the probability of dying of the total cohort. Unless it is possible to follow-up a cohort, as was done in Donora, this probability can be estimated only approximately. It will be noted that, if P_s were used in its stead, the value of P_t would be overestimated when the mortality of the moved was less than the mortality of those who did not move, and that the value of P_t would be underestimated when the mortality of the moved was higher than that of those who did not move.

Several ways have been suggested for estimating the probability of dying when complete information on the persons who have moved is not available. For example, there is the time-honoured approach used in life-table construction in which the population at risk at the beginning of the interval is reduced by one-half of the persons who moved during the interval. With this approach,

$$\hat{P}_i = \frac{d_i}{1_i - \frac{1}{2}m_i},$$

when d_i = observed deaths and m_i = the number moved (lost to follow-up) during the period, and 1_i = the number at risk at the beginning of the period. For w periods of follow-up we may define P_a as follows:

$$P_a = 1 - \overset{w}{\pi}(1 - \hat{P}_i).$$

If, as is often the case, information is not available regarding the dates of movement and subsequent mortality, and if there is only information on the number of persons at the initial observation period, the numbers who moved, and the numbers who died in the place of residence, only an over-all mortality rate for the total interval of follow-up can be calculated by following the suggested approach. The rates calculated in this manner (P_s, P_a) may be denoted, respectively;

$$P^{\circ}{}_s = \frac{d}{d + s}$$

$$P^{\circ}{}_a = \frac{d}{n - \frac{1}{2}m}$$

where: n is the size of the original cohort
d is the total number of observed deaths
s is the number of survivors among those who have not moved,
m is the number of persons who have moved (lost to follow-up) during the total period of follow-up.

The values of P_s, P_a, $P^{\circ}{}_a$, $P^{\circ}{}_s$, calculated on the 1948–1957 experience of the Donora sample, are compared with P_t in Table III; and the values of P_s and P_a calculated on the one year experience (1951–1952) of the Arsenal sample are compared with P_t in Table IV.

TABLE III

COMPARISON OF VARIOUS ESTIMATES OF THE PROBABILITY OF DYING, DONORA SAMPLE, 1948–1957, ACCORDING TO SEX, AGE, AND ILLNESS STATUS IN 1948

Probability of Dying	Male				Female			
	Age 21–49		Age 50 and Over		Age 21–49		Age 50 and Over	
	Ill	Not Ill	Ill	Not Ill	Ill	Not Ill	Ill	Not Ill
P_t	0·0449	0·0173	0·2681	0·2278	0·0398	0·0145	0·2428	0·1871
P_s	0·0506	0·0193	0·2791	0·2327	0·0438	0·0173	0·2467	0·1878
P_a	0·0513	0·0196	0·2784	0·2351	0·0445	0·0175	0·2488	0·1829
$P^{\circ}{}_a$	0·0500	0·0194	0·2772	0·2321	0·0438	0·0164	0·2511	0·1813
$P^{\circ}{}_s$	0·0565	0·0220	0·2907	0·2500	0·0488	0·0188	0·2701	0·1875

TABLE IV

COMPARISON OF VARIOUS ESTIMATES OF THE PROBABILITY OF DYING, ARSENAL SAMPLE, 1951–1952 AND 1951–1956, ACCORDING TO SEX, AGE, AND ILLNESS STATUS IN 1951

Period	Probability of Dying	Male				Female			
		Age 21–49		Age 50 and Over		Age 21–49		Age 50 and Over	
		Ill	Not Ill	Ill	Not Ill	Ill	Not Ill	Ill	Not Ill
1951–2	P_t	0·0089	0·0059	0·0772	0·0178	0·0080	0·0006	0·0277	0·0244
	P_s	0·0103	0·0069	0·0794	0·0189	0·0000	0·0000	0·0270	0·0209
	P_a	0·0094	0·0063	0·0761	0·0183	0·0000	0·0000	0·0258	0·0202
1951–6	$P^{\circ}{}_a$	0·0337	0·0150	0·2687	0·1187	0·0279	0·0022	0·1064	0·0806
	$P^{\circ}{}_s$	0·0472	0·0210	0·3195	0·1422	0·0400	0·0030	0·1318	0·0982

The data of Table III reveal immediately that, in comparison with P_t, the "true" mortality rate for the $8\frac{1}{2}$-year period, the other calculated rates are higher in most instances. The estimate, $P^{\circ}{}_s$, has the largest discrepancy, obviously because it entirely overlooks the moved in the denominator. On the other hand, when the rates are calculated annually, based only on the persons who stayed in Donora (P_s), the magnitude of the deviation from P_t is about equal to if not smaller than that observed when P_a or $P^{\circ}{}_a$ is computed. It is interesting to note that the difference between $P^{\circ}{}_a$ and P_t is more often smaller than the difference between P_a and P_t. Similar comparisons are possible on the Arsenal sample for the one-year interval 1951–52.

The data of Table IV show that in this instance the differences between P_a and P_t are more often smaller than the difference between P_s and P_t.

The implication of these comparisons will be discussed elsewhere. Here it is sufficient to point out that the differences between the several rates compared are in part due to differences in the frequency of movement within the time intervals studied. Consequently, estimation procedures for mortality or other rates become purely arithmetical exercises unless they take into account the actual behaviour of disturbing factors such as movement in the above example.

It is of interest to note from Tables III and IV that the difference between corresponding rates for the "ill" and "not ill" or the ratio of the corresponding rates indicates that the differences or ratios based on P_t are closely approximated by differences or ratios based on the various approximations. In other words, as the events of movement occurred in the Donora Sample for the period 1948–57 and in the Arsenal Sample for the period 1951–2, the approximation usually employed to calculate mortality when there is loss in the population at risk (here indicated as P_a) may overestimate or underestimate the actual mortality rates of the ill and not ill by a considerable amount. However, as it happens, these approximations do not seem to distort too much the difference between the two groups.

Sampling Variation

Chance fluctuations in all the rates we have described must be considered when contrasting the ill group with the not ill group. To employ a parametic test for this purpose requires calculation of the variance. If we follow accepted procedures, the variance of the estimated P_t may be taken simply as $P_t(1 - P_t)/n$, where n is the original size of the group considered. For rates such as P_a, in which corrections are made for the reduction in the size of the original cohort, a formula suggested by Irwin (1949) may be used. The difference in mortality rates for corresponding ill and not ill groups, when divided by the estimated variance of the difference, will be approximately normally distributed with zero mean and unit variance under the "null hypothesis".

From the data of Tables III and IV we have carried out tests of the differences between mortality rates for corresponding ill and not ill groups, based on P_t for 1948–57, for the Donora sample, and on P_t for 1951–52, and $P^{\circ}{}_a$ for 1951–56, for the Arsenal sample. The results of the tests show that the observed difference would occur by chance less than once in a hundred in the cases of:

(*a*) Donora males and females in the age group 21–49;

(*b*) Arsenal males of 50 years and over, when P_t for 1951–52, is compared;

(*c*) Arsenal males of 50 years and over and females of 21–49 years when $P^{\circ}{}_a$, for 1951–56 is compared.

For the other age and sex groups on which the tests have been made the differences are apparently not large enough to reach statistical significance in terms of the stated criterion for sampling variation.

The whole question of testing group differences for follow-up data of the type reported here is, of course, dependent upon the specific objectives of the analysis. Differences in the cumulative mortality between the two groups up to some point of time in the follow-up period may be of interest for one purpose; differences in the annual mortality may be of interest for another. Perhaps, most generally, we would seek for a representation of the entire phenomenon in terms of the cumulative probability distribution function of the time at death to determine whether the two groups have different distributions and what the magnitudes of the differences are.

To our knowledge, an adequate discussion of the problems of determining the proper variance expressions, the "effective" sample size, the forms of the distribution functions, choice of test criteria, etc., which are appropriate for follow-up investigations has not as yet appeared in the literature. In subsequent papers of this series we hope to examine this aspect of the analysis of cohort data in greater detail.

Discussion

The relationship of reported illness and subsequent mortality and change of residence has been

examined (*a*) for the interval 1948–1957 in a sample of 2,712 persons aged 21 years and over residing and surveyed in Donora, Pa, in 1948; and (*b*) for the interval 1951–1956 in a sample of 6,305 persons aged 21 years and over residing and surveyed in the Arsenal Health District of Pittsburgh, Pa, in 1951. The survey of Donora in 1948 was undertaken to investigate the sickness effects of the smog episode of October of that year. The survey of the Arsenal District in 1951 was undertaken to determine the frequency of illness and the receipt of medical care in the population.

The analyses discussed in this paper seek to answer only two questions:

(1) Did persons who reported illness change their address or die at a different rate from persons who did not?

(2) To what extent is the estimate of mortality affected by the differential mobility?

In answer to the first question, the data reveal:

(1) There was no consistent difference in the frequency of change of address between those who reported illness at the initial survey and those who did not.

(2) In general, persons who reported some illness at the initial survey had a higher mortality than those who did not.

(*a*) For the Donora data for which annual mortality rates could be estimated, the difference showed a tendency to become smaller with length of time.

(*b*) The difference between the mortality of those who reported illness at the initial survey and those who did not may be due to chance variation for certain age-sex subgroups. However, a thorough investigation of the role of chance in the observed differences has not been undertaken.

While a full interpretation of these findings requires further analysis of the data, certain inferences may be drawn now. It appears that observations such as these made by eliciting information on sickness complaints through interviews does identify persons who for some time will have a higher risk of dying than others. Taking into consideration the Hagerstown study already mentioned and the findings of the Donora sample, we could conclude that the duration of this higher risk has an optimum point.

If it were true that identification of persons with a greater risk of mortality for a specified interval of time can be made through the interview type of survey, this approach could be used to throw light on the patterns of sickness which lead to death and also to provide an earlier starting point for studies aimed at exploring antecedent factors in sickness. Further analysis of the present material, particularly with respect to the relationship of specific sickness to specific cause of death, and of specific sickness in successive observations, is required before a final interpretation can be made of the findings here reported.

In answer to the second question, the Donora data indicate that estimates in which an adjustment is made for loss of data due to change of residence, or in which this loss is disregarded, may vary considerably from the rate based on knowledge about the total cohort. Although, in this particular sample, the different estimates did not affect the differences in mortality rate between those who reported illness at the initial survey and those who did not, it is clear that the usual methods of estimating mortality rates for a cohort that has been affected in the course of time by a loss of persons under observation may give rather crude approximations. Our data have shown that the differential rate of mortality among those who move as well as the varying proportions of persons who move will produce departures from the actual mortality rate that cannot be compensated for by the adjustment procedures now employed.

The observations and points discussed only hint at some of the major questions which must be resolved before we can undertake with assurance the analysis of long-term or cohort data. It is hoped that as more such data are collected greater efforts will be made to re-examine critically the pertinent analytical procedures.

Summary

Data on reported illness, subsequent mortality, and change of residence from two follow-up studies of approximately 9,000 adult persons have been analysed for relations between reported illness status and subsequent mobility or subsequent mortality. These analyses show (1) no consistent or clear-cut relation between reported illness status and later mobility, and (2) higher subsequent mortality among persons reported ill than among persons reported not ill. Various methods of estimating the subsequent mortality in the ill and not-ill group, which utilize different assumptions concerning mortality within the groups lost to follow-up through movement, are compared with the rate based on complete mortality knowledge about the total cohort.

REFERENCES

Berkson, J. (1955). *Proc. Mayo Clin.*, **30**, 319.

Ciocco, A. (1946). *Hum. Biol.*, **18**, 33.

—— and Lawrence, P. S. (1952). In "Illness and Health Services in an Ageing Population", by G. St. U. Perrott, A. Ciocco, G. Baehr, L. S. Rosenfeld, and Their Collaborators, p. 26 (Public Health Service Publication, No. 170). Washington, D.C., U.S.A.

Cobb, S., Thompson, D. J., Rosenbaum, J., Warren, J. E., and Merchant, W. R. (1956). *J. chron. Dis.*, **3**, 134.

Horvitz, D. G. (1952). *Publ. Hlth Rep.* (*Wash.*), **67**, 1003.

Kodlin, D., and Thompson, D. J. (1958). "An Appraisal of the Longitudinal Approach to Studies of Growth and Development". *Monogr. Soc. Res. Child Developm.*, **23**, 1. (Serial No. 67).

Lawrence, P. S. (1948). *Publ. Hlth Rep.* (*Wash.*), **63**, 69.

Logan, W. P. D., and Brookes, E. M. (1957). "The Survey of Sickness, 1943–1952". General Register Office. Studies on Medical and Population Subjects, No. 12. H.M.S.O., London.

Schrenk, H. H., Heimann, H., Clayton, G. D., Gafafer, W. M., and Wexler, H. (1949). "Air Pollution in Donora, Pa: Epidemiology of the Unusual Smog Episode of October, 1948. Preliminary Report" (Public Health Bulletin, No. 306). Washington, D.C., U.S.A.

Tauber, J., and Thompson, D. J. (1957). *J. chron. Dis.*, **6**, 595.

Brit. J. prev. soc. Med. (1958), **12**, 183–187

GENOTYPIC FREQUENCIES AMONG CLOSE RELATIVES OF PROPOSITI WITH CONDITIONS DETERMINED BY X-RECESSIVE GENES

BY

GEORGE KNOX*

From the Department of Social Medicine, University of Birmingham

The investigation of human abnormalities suspected of possessing genetic determinants demands algebra more complicated than that which may be useful in experimental studies. This is because of the selective effects invoked when we begin with an affected individual and work backwards towards his ancestors and collateral relatives.

In the course of another study the problem arose of the expected genotypic frequencies in the close relatives of children suffering from a condition supposedly determined by an X-recessive gene. Since the results of the necessary deductions may be useful in other population studies of sex-linkage, and since the results do not seem to be available elsewhere, it seemed worthwhile to present them in a separate paper.

(*a*) Sex Ratio in Propositi

If an X-recessive gene, $\dot{X}$, has a frequency g, then the population frequency of males of the genotype $\dot{X}Y$ is g, and of females of genotype $\dot{X}\dot{X}$ it is g^2. Consequently, the ratio $F/M = g^2/g = g$, and when the genotypes are fully penetrant or equally penetrant, the sex ratio provides a direct measure of the gene frequency. An alternative expression in these circumstances is that the proportion of females among propositi is $\frac{g}{1+g}$ and of males it is $\frac{1}{1+g}$.

(*b*) Genotypes of Parents

The Mother

Whether the propositus is a boy or a girl we know a gene $\dot{X}$ was received from the mother, who must be either $X\dot{X}$ or $\dot{X}\dot{X}$. The respective population frequencies of these genotypes in women are $2g(1-g)$ and g^2. The second genotype, however, has a doubled opportunity of transmitting the gene $\dot{X}$ to any particular child, so the relative frequencies of the two genotypes in mothers of affected children are $2g(1-g)$ and $2g^2$, and the absolute frequencies are $(1-g)$ and g.

The Father

When the propositus is a girl we know the father is $\dot{X}Y$.

When the propositus is a boy we have no information upon the father's genotype and can presume that the genotypes XY and $\dot{X}Y$ occur in the same proportional probabilities as in the population, that is $(1-g)$ and g.

If we presume that the sex ratio of propositi is equal to the gene frequency, we may conclude that the fathers' genotypes for all affected children are:

$$\dot{X}Y = 2g/(1+g), \quad \text{and} \quad XY = (1-g)/(1+g).$$

More usefully, perhaps, the frequencies of mating-types among parents may be stated as in Table I.

TABLE I
MATING TYPE FREQUENCIES

Affected Children	Parental Genotypes	Frequency
Boys	$\dot{X}\dot{X}-\dot{X}Y$	g^2
	$X\dot{X}-\dot{X}Y$	$g(1-g)$
	$\dot{X}\dot{X}-XY$	$g(1-g)$
	$X\dot{X}-XY$	$(1-g)^2$
Girls	$\dot{X}\dot{X}-\dot{X}Y$	g
	$X\dot{X}-\dot{X}Y$	$(1-g)$
All Children (presuming that $F/M=g$)	$\dot{X}\dot{X}-\dot{X}Y$	$2g^2/(1+g)$
	$X\dot{X}-\dot{X}Y$	$g(1-g)/(1+g)$
	$\dot{X}\dot{X}-XY$	$2g(1-g)/(1+g)$
	$X\dot{X}-XY$	$(1-g)^2/(1+g)$

* Medical Research Council Clinical Research Fellow.

TABLE II

SUBSEQUENT SIBLINGS OF AFFECTED GIRLS (METHOD)

Parental Mating Combinations		Expected Progeny Frequencies		Genotypes of Subsequent Siblings
Type	Frequency	Of Boys	Of Girls	
$\dot{X}\dot{X}-\dot{X}Y$ ..	g	XY .. 0 $\dot{X}Y$ .. 1	XX .. 0 $X\dot{X}$ .. 0 $\dot{X}\dot{X}$ .. 1	*Brothers* $XY=g\times 0+(1-g)\times\frac{1}{2}=(1-g)/2$ $\dot{X}Y=g\times 1+(1-g)\times\frac{1}{2}=(1+g)/2$
$X\dot{X}-\dot{X}Y$ ..	$(1-g)$	XY .. $\frac{1}{2}$ $\dot{X}Y$ .. $\frac{1}{2}$	XX .. 0 $X\dot{X}$ .. $\frac{1}{2}$ $\dot{X}\dot{X}$ .. $\frac{1}{2}$	*Sisters* $XX=g\times 0+(1-g)\times 0=0$ $X\dot{X}=g\times 0+(1-g)\times\frac{1}{2}=(1-g)/2$ $\dot{X}\dot{X}=g\times 1+(1-g)\times\frac{1}{2}=(1+g)/2$

Subsequent Siblings of Boys

XY $(1-g)/2$
$\dot{X}Y$ $(1+g)/2$ } of subsequent brothers

XX $(1-g)^2/2$
$X\dot{X}$ $(1-g)(1+2g)/2$
$\dot{X}\dot{X}$ $g(1+g)/2$ } of subsequent sisters.

Subsequent Siblings of all Propositi
(presuming that $F/M=g$)

$XY=(1-g)/2$
$\dot{X}Y=(1+g)/2$ } of subsequent brothers

$XX=(1-g)^2/2(1+g)$
$X\dot{X}=(1-g)(1+3g)/2(1+g)$
$\dot{X}\dot{X}=g$ } of subsequent sisters.

(*c*) GENOTYPES OF SUBSEQUENT SIBLINGS

From the frequencies of parental mating combinations given above together with the expected genotype frequencies in the progeny of each combination, we may deduce the absolute frequencies of different genotypes in subsequent siblings of affected children. The procedure is illustrated fully for affected girls in Table II and the results for boys and for girls + boys are given in the footnotes thereto.

It is interesting to note also that, when two cases of disease occur in each of a series of sibships, the relative proportion of MM, MF, FM, and FF pairs are calculable from the products of the population relative frequencies of the first and the appropriate value for subsequent sibs as given above. This gives:

$$\begin{aligned} MM &= (1+g)/2 \\ MF+FM &= 2g(1+g)/2 \\ FF &= g(1+g)/2. \end{aligned}$$

From this the absolute frequencies of pairs of the three types are:

$$\begin{aligned} MM &= 1/(1+3g) \\ MF+FM &= 2g/(1+3g) \\ FF &= g/(1+3g). \end{aligned}$$

It is clear from this that, in sex-linked inheritance with equal penetrance in the two sexes, the ratio $(FM+MF)/FF$ is 2 at all gene frequencies and that the ratio FF/MM is equal to g. An alternative estimator of g, using all the pair-data, is

$$(FM+MF+FF)/3MM.$$

(*d*) GENOTYPES OF MATERNAL GRANDPARENTS

We have seen that the mother of an affected child of either sex is $X\dot{X}$ on $(1-g)$ occasions and $\dot{X}\dot{X}$ on g occasions.

When she is $\dot{X}\dot{X}$, the reasoning given under (*b*) can be re-applied; the probability of *her* parents being $\dot{X}\dot{X}-\dot{X}Y$ is g, and of their being $X\dot{X}-\dot{X}Y$ is $(1-g)$, no other combinations being possible. Thus, the probability that an affected child will have an $\dot{X}\dot{X}$ mother with maternal grandparents $\dot{X}\dot{X}-\dot{X}Y$ is g^2, and an $\dot{X}\dot{X}$ mother with maternal grandparents $X\dot{X}-\dot{X}Y$ is $g(1-g)$.

When she is $X\dot{X}$ her own parents may be as shown in Table III.

TABLE III

PARENTS OF AN $X\dot{X}$ MOTHER

Genotype	Absolute Population Frequencies	Relative Population Frequencies
$\dot{X}\dot{X}-XY$	$g^2(1-g)$	g
$X\dot{X}-XY$	$2g(1-g)^2$	$2(1-g)$
$X\dot{X}-\dot{X}Y$	$2g^2(1-g)$	$2g$
$XX-\dot{X}Y$	$g(1-g)^2$	$(1-g)$

However, the first and last of these combinations have twice the chance of the others of transmitting the genotype $\dot{X}X$ to any particular daughter, so that the relative frequencies among parents of $X\dot{X}$ women become g, $(1-g)$, g, $(1-g)$, respectively, and the absolute frequencies are half these values. The probability of an affected child having an $X\dot{X}$ mother *and* grandparents of these types are the products of these last (halved) values with $(1-g)$.

Since we may not be able to distinguish between $X\dot{X}$ and $\dot{X}\dot{X}$ mothers we may add these results together in the appropriate proportions. The resulting frequencies for maternal grandparents mating types are then as follows:

Mating Type	*Frequency*
$\dot{X}\dot{X}-\dot{X}Y$	g^2
$\dot{X}\dot{X}-X\dot{Y}$	$g(1-g)/2$
$X\dot{X}-\dot{X}Y$	$3g(1-g)/2$
$X\dot{X}-X\dot{Y}$	$(1-g)^2/2$
$XX-\dot{X}Y$	$(1-g)^2/2$.

(*e*) Genotypes of Maternal Aunts and Uncles

Proceeding in a manner analagous with the reasoning under (*c*), multiplying expected progeny frequencies by the above frequencies of grandparental mating-types, we may obtain the genotype frequencies in maternal aunts and uncles. These are:

$$\left.\begin{aligned} X\dot{Y} &= 3(1-g)/4 \\ \dot{X}Y &= (1+3g)/4 \end{aligned}\right\} \text{ of maternal uncles}$$

$$\left.\begin{aligned} XX &= (1-g)^2/4 \\ X\dot{X} &= (1-g)(3+2g)/4 \\ \dot{X}\dot{X} &= g(3+g)/4 \end{aligned}\right\} \text{ of maternal aunts.}$$

This is the same whether the propositus is a boy or a girl.

(*f*) Genotypes of Maternal Cousins

Maternal uncles will engage in marriages of the following types and frequencies:

Mating Type	*Frequency*
$\dot{X}\dot{X}$ $\dot{X}Y$	$g^2(1+3g)/4$
$X\dot{X}$ $\dot{X}Y$	$2g(1-g)(1+3g)/4$
XX $\dot{X}Y$	$(1-g)^2(1+3g)/4$
$\dot{X}\dot{X}$ $X\dot{Y}$	$3g^2(1-g)/4$
$X\dot{X}$ $X\dot{Y}$	$6g(1-g)^2/4$
XX $X\dot{Y}$	$3(1-g)^2/4$.

By applying expected progeny ratios for these matings, we expect the following genotypic frequencies among their offspring (*i.e.* cousins of propositi):

$$\left.\begin{aligned} X\dot{Y} &= (1-g) \\ \dot{X}Y &= g \end{aligned}\right\} \text{ of sons of maternal uncles}$$

$$\left.\begin{aligned} XX &= 3(1-g)^2/4 \\ X\dot{X} &= (1-g)(1+6g)/4 \\ \dot{X}\dot{X} &= g(1+3g)/4 \end{aligned}\right\} \text{ of daughters of maternal uncles.}$$

Maternal aunts will engage in the same six types of marriages but with frequencies:

Mating Type	*Frequency*
$\dot{X}\dot{X}$ $\dot{X}Y$	$g^2(3+g)/4$
$X\dot{X}$ $\dot{X}Y$	$g(1-g)(3+2g)/4$
XX $\dot{X}Y$	$g(1-g)^2/4$
$\dot{X}\dot{X}$ $X\dot{Y}$	$g(1-g)(3+g)/4$
$X\dot{X}$ $X\dot{Y}$	$(1-g)^2(3+2g)/4$
XX $X\dot{Y}$	$(1-g)^2/4$.

In the same way as for maternal uncles we may deduce the genotype frequencies in the offspring of the maternal aunts as follows:

$$\left.\begin{aligned} X\dot{Y} &= 5(1-g)/8 \\ \dot{X}Y &= (3+5g)/8 \end{aligned}\right\} \text{ of sons of maternal aunts}$$

$$\left.\begin{aligned} XX &= 5(1-g)^2/8 \\ X\dot{X} &= (3+10g)(1-g)/8 \\ \dot{X}\dot{X} &= g(3+5g)/8 \end{aligned}\right\} \text{ of daughters of maternal aunts.}$$

Maternal cousins of all kinds, *via* uncles or aunts, are distributed as follows:

$$\left.\begin{aligned} X\dot{Y} &= 13(1-g)/16 \\ \dot{X}Y &= (3+13g)/16 \end{aligned}\right\} \text{ of all male maternal cousins}$$

$$\left.\begin{aligned} XX &= 11(1-g)^2/16 \\ X\dot{X} &= (1-g)(5+22g)/16 \\ \dot{X}\dot{X} &= g(5+11g)/16 \end{aligned}\right\} \text{ of all female maternal cousins.}$$

All the values given in this section are the same for male propositi as for females.

(*g*) Genotypes of Paternal Grandparents

On the $1/(1+g)$ occasions when the propositus is male, the genotypes of paternal grandparents may be taken as representative of the population as a whole, and the various pair combinations likewise, that is:

Mating Type	*Frequency*
$\dot{X}\dot{X}-\dot{X}Y$	g^3
$X\dot{X}-\dot{X}Y$	$2g^2(1-g)$
$XX-\dot{X}Y$	$g(1-g)^2$
$\dot{X}\dot{X}-XY$	$g^2(1-g)$
$X\dot{X}-XY$	$2g(1-g)^2$
$XX-XY$	$(1-g)^3$

. . . and all aunts, uncles, and cousins in these families may be regarded as being distributed as in the normal population, that is:

$$\left.\begin{aligned} XY &= (1-g) \\ \dot{X}Y &= g \end{aligned}\right\} \text{ of all males}$$

$$\left.\begin{aligned} XX &= (1-g)^2 \\ X\dot{X} &= 2g(1-g) \\ \dot{X}\dot{X} &= g^2 \end{aligned}\right\} \text{ of all females.}$$

On the $g/(1+g)$ occasions when the propositus is female, we know that the father is $\dot{X}Y$; in this event the same argument applies to the paternal grandparents as was applied to the parental genotypes of male propositi under (*b*). Thus, the combination frequencies of the paternal grandparents of female propositi are:

$$\dot{X}\dot{X}-\dot{X}Y = g^2$$
$$\dot{X}\dot{X}-XY = g(1-g)$$
$$X\dot{X}-\dot{X}Y = g(1-g)$$
$$X\dot{X}-XY = (1-g)^2 \text{ (}i.e.\text{ as the parents of affected boys. See (}b\text{))}.$$

If we fail to distinguish between male and female propositi and presume that the F/M ratio $=g$, the genotypes of all paternal grandparents are:

Mating Type	*Frequency*
$\dot{X}\dot{X}-\dot{X}Y$	$2g^3/(1+g)$
$X\dot{X}-\dot{X}Y$	$3g^2(1-g)/(1+g)$
$XX-\dot{X}Y$	$g(1-g)^2/(1+g)$
$\dot{X}\dot{X}-XY$	$2g^2(1-g)/(1+g)$
$X\dot{X}-XY$	$3g(1-g)^2/(1+g)$
$XX-XY$	$(1-g)^3/(1+g)$.

(*h*) Genotypes of Paternal Aunts and Uncles

Paternal uncles and aunts of male propositi have genotype frequencies equal to those in the population.

The paternal uncles and aunts of female propositi have genotype frequencies calculable from the frequency of mating types in the paternal grandparents (see (*g*)). The genotypes of these uncles and aunts are the same as for later sibs of male propositi, (see (*b*)) namely:

$\left.\begin{matrix}\dot{X}Y=(1-g)/2\\ \dot{X}Y=(1+g)/2\end{matrix}\right\}$ of paternal uncles of female propositi

$\left.\begin{matrix}X\dot{X}=(1-g)^2/2\\ X\dot{X}=(1-g)\,(1+2g)/2\\ \dot{X}\dot{X}=g(1+g)/2\end{matrix}\right\}$ of paternal aunts of female propositi.

The distribution for all paternal aunts and uncles, irrespective of the sex of the propositus, and presuming F/M $=g$, is:

$\left.\begin{matrix}\dot{X}Y=(2+g)\,(1-g)/2(1+g)\\ \dot{X}Y=g(3+g)/2(1+g)\end{matrix}\right\}$ of all paternal uncles

$\left.\begin{matrix}X\dot{X}=(2+g)\,(1-g)^2/2(1+g)\\ X\dot{X}=g(1-g)\,(5+2g)/2(1+g)\\ \dot{X}\dot{X}=g^2(3+g)/2(1+g)\end{matrix}\right\}$ of all paternal aunts.

(*i*) Genotypes of Paternal Cousins

Paternal cousins of male propositi have genotype frequencies equal to those in the population (see (*g*)).

Paternal cousins of female propositi have genotype frequencies based upon the frequency of mating types entered into by uncles and aunts of genotype frequencies given under (*h*). These mating frequencies are as follows:

	Mating Type	*Frequency*
For Paternal Uncles of Females	$\dot{X}\dot{X}-\dot{X}Y$	$g^2(1+g)/2$
	$X\dot{X}-\dot{X}Y$	$2g(1-g)\,(1+g)/2$
	$XX-\dot{X}Y$	$(1-g)^2(1+g)/2$
	$\dot{X}\dot{X}-XY$	$g^2(1-g)/2$
	$X\dot{X}-XY$	$2g(1-g)^2/2$
	$XX-XY$	$(1-g)^3/2$
For Paternal Aunts of Females	$\dot{X}\dot{X}-\dot{X}Y$	$g^2(1+g)/2$
	$X\dot{X}-\dot{X}Y$	$g(1-g)\,(1+2g)/2$
	$XX-\dot{X}Y$	$g(1-g)^2/2$
	$\dot{X}\dot{X}-XY$	$g(1+g)\,(1-g)/2$
	$X\dot{X}-XY$	$(1-g)^2(1+2g)/2$
	$XX-XY$	$(1-g)^3/2$
For All Paternal Aunts and Uncles of Females	$\dot{X}\dot{X}-\dot{X}Y$	$g^2(1+g)/2$
	$X\dot{X}-\dot{X}Y$	$g(1-g)\,(3+4g)/4$
	$XX-\dot{X}Y$	$(1+2g)\,(1-g)^2/4$
	$\dot{X}\dot{X}-XY$	$g(1-g)\,(1+2g)/4$
	$X\dot{X}-XY$	$(1+4g)\,(1-g)^2/4$
	$XX-XY$	$(1-g)^3/2$
For All Paternal Aunts and Uncles of All Propositi when F/M $=g$	$\dot{X}\dot{X}-\dot{X}Y$	$g^2(3+g)/2(1+g)$
	$X\dot{X}-\dot{X}Y$	$g^2(1-g)\,(11+4g)/4(1+g)$
	$XX-\dot{X}Y$	$g(1-g)^2\,(5+2g)/4(1+g)$
	$\dot{X}\dot{X}-XY$	$g^2(1-g)\,(5+2g)/4(1+g)$
	$X\dot{X}-XY$	$g(1-g)^2(9+4g)/4(1+g)$
	$XX-XY$	$(1-g)^3(2+g)/2(1+g)$.

From these formulae, by a variety of routes, the genotypes of paternal cousins may be deduced:

Children of Paternal Uncles of Females

$\left.\begin{matrix}XY=(1-g)\\ \dot{X}Y=g\end{matrix}\right\}$ of sons of paternal uncles of females

$\left.\begin{matrix}XX=(1-g)^2/2\\ X\dot{X}=(1-g)\,(1+2g)/2\\ \dot{X}\dot{X}=g(1+g)/2\end{matrix}\right\}$ of daughters of paternal uncles of females

(*Note:* The boy cousins here are distributed as in the normal population. The girl cousins are similar to the later sisters of male propositi (c) and to the paternal aunts of female propositi. The paternal aunts of female propositi are also the paternal aunts of the girl cousins themselves.)

Children of Paternal Aunts of Females

$\left.\begin{matrix}XY=3(1-g)/4\\ \dot{X}Y=(1+3g)/4\end{matrix}\right\}$ of sons of paternal aunts of females

$\left.\begin{matrix}XX=3(1-g)^2/4\\ X\dot{X}=(1-g)\,(1+6g)/4)\\ \dot{X}\dot{X}=g(1+3g)/4\end{matrix}\right\}$ of daughters of paternal aunts of females

All Paternal Cousins of Females

$\left.\begin{matrix}XY=7(1-g)/8\\ \dot{X}Y=(1+7g)/8\end{matrix}\right\}$ of sons of paternal aunts and uncles of females

$\left.\begin{matrix}XX=5(1-g)^2/8\\ X\dot{X}=(1-g)\,(3+10g)/8\\ \dot{X}\dot{X}=g(3+5g)/8\end{matrix}\right\}$ of daughters of paternal aunts and uncles of females

Children of Paternal Uncles of All Propositi when F/M $=g$

$\left.\begin{matrix}XY=1-g\\ \dot{X}Y=g\end{matrix}\right\}$ of sons of all paternal uncles

$\left.\begin{matrix}XX=(2+g)\,(1-g)^2/2\,(1+g)\\ X\dot{X}=g(1-g)\,(5+2g)/2\,(1+g)\\ \dot{X}\dot{X}=g^2(3+g)/2\,(1+g)\end{matrix}\right\}$ of daughters of all paternal uncles

Children of Paternal Aunts of All Propositi when F/M $=g$

$\left.\begin{matrix}XY=(1-g)\,(4+3g)/4\,(1+g)\\ \dot{X}Y=g(5+3g)/4\,(1+g)\end{matrix}\right\}$ of sons of all paternal aunts

$\left.\begin{matrix}XX=(4+3g)\,(1-g)^2/4\,(1+g)\\ X\dot{X}=3g(1-g)\,(3+2g)/4\,(1+g)\\ \dot{X}\dot{X}=g^2(5+3g)/4\,(1+g)\end{matrix}\right\}$ of daughters of all paternal aunts

All Paternal Cousins of All Propositi when F/M $=g$

$\left.\begin{matrix}XY=(1-g)\,(8+7g)/8\,(1+g)\\ \dot{X}Y=g(9+7g)/8\,(1+g)\end{matrix}\right\}$ of all male cousins of all propositi

$\left.\begin{matrix}XX=(1-g)^2(8+5g)/8\,(1+g)\\ X\dot{X}=g(1-g)\,(19+10g)/8\,(1+g)\\ \dot{X}\dot{X}=g^2(11+5g)/8\,(1+g)\end{matrix}\right\}$ of all female cousins of all propositi.

(*j*) Examples

Several worked examples of the application of these formulae are given in Table IV. It is shown there that, at the upper limit of g, all the formulae resolve into the same values. It will be sufficiently clear at what steps the combination of data for male and female propositi depends upon the assumption that $F/M = g$ and when the combination of data related to aunts and uncles depends upon the assumption that both occur in equal numbers. It is also implicit in the construction that major selective effects (for example the death of males) have not distorted the picture, and mutations have not been taken into account.

Summary

The algebraic implications of sex-linked transmission are explored from the point of view that propositi have been selected and the genotypic frequencies in relatives are to be deduced. Formulae are presented for the expected frequencies in relatives. Some numerical examples are also given.

Table IV

TABULATED FREQUENCIES OF GENOTYPES OF MAIN RELATIVES OF PROPOSITI AT DIFFERENT VALUES OF g

Relative	Sex of Propositus	Genotype	g				
			Nr. 0·0	0·1	0·2	0·5	Nr 1·0
Later Sibs	M	XY	0·5	0·45	0·4	0·25	0·0
		XY	0·5	0·55	0·6	0·75	1·0
		XX	0·5	0·405	0·32	0·125	0·0
		XX	0·5	0·54	0·56	0·5	0·0
		XX	0·0	0·055	0·12	0·375	1·0
Later Sibs	F	XY	0·5	0·45	0·4	0·25	0·0
		XY	0·5	0·55	0·6	0·75	1·0
		XX	0·0	0·0	0·0	0·0	0·0
		XX	0·5	0·45	0·4	0·25	0·0
		XX	0·5	0·55	0·6	0·75	1·0
Later Sibs	M + F (F/M = *g*)	XY	0·5	0·45	0·4	0·25	0·0
		XY	0·5	0·55	0·6	0·75	1·0
		XX	0·5	0·368	0·267	0·083	0·0
		XX	0·5	0·532	0·533	0·417	0·0
		XX	0·0	0·1	0·2	0·5	1·0
Maternal Uncles and Aunts ..	M or F or M + F	XY	0·75	0·675	0·6	0·375	0·0
		XY	0·25	0·325	0·4	0·625	1·0
		XX	0·25	0·202	0·16	0·062	0·0
		XX	0·75	0·72	0·68	0·5	0·0
		XX	0·0	0·077	0·16	0·437	1·0
Maternal Cousins	M or F or M + F	XY	0·813	0·732	0·65	0·406	0·0
		XY	0·187	0·269	0·35	0·594	1·0
		XX	0·687	0·557	0·44	0·172	0·0
		XX	0·313	0·405	0·47	0·5	0·0
		XX	0·0	0·038	0·09	0·328	1·0
Paternal Uncles and Aunts ..	F	XY	0·5	0·45	0·4	0·25	0·0
		XY	0·5	0·55	0·6	0·75	1·0
		XX	0·5	0·405	0·32	0·125	0·0
		XX	0·5	0·54	0·56	0·5	0·0
		XX	0·0	0·055	0·12	0·375	1·0
Paternal Uncles and Aunts ..	M + F (F/M = *g*)	XY	1·0	0·859	0·733	0·417	0·0
		XY	0·0	0·141	0·267	0·583	1·0
		XX	1·0	0·773	0·587	0·208	0·0
		XX	0·0	0·213	0·36	0·5	0·0
		XX	0·0	0·014	0·053	0·292	1·0
Paternal Cousins	F	XY	0·875	0·788	0·7	0·437	0·0
		XY	0·125	0·212	0·3	0·563	1·0
		XX	0·625	0·506	0·4	0·156	0·0
		XX	0·375	0·45	0·5	0·5	0·0
		XX	0·0	0·044	0·1	0·344	1·0
Paternal Cousins	M + F (F/M = *g*)	XY	1·0	0·89	0·783	0·479	0·0
		XY	0·0	0·11	0·217	0·521	1·0
		XX	1·0	0·782	0·6	0·219	0·0
		XX	0·0	0·205	0·35	0·5	0·0
		XX	0·0	0·013	0·05	0·281	1·0

The frequencies in this Table refer to 1·0 = Total individuals *of the same sex*

Brit. J. prev. soc. Med. (1958), **12**, 188–192

ON THE NATURE OF THE DETERMINANTS OF CONGENITAL PYLORIC STENOSIS

BY

GEORGE KNOX*

From the Department of Social Medicine, University of Birmingham

A comprehensive hypothesis of the aetiology of congenital pyloric stenosis must account for a number of striking and well established features. They include a differential sex incidence, the disease being four to five times more frequent in boys than in girls; a falling incidence with increasing birth rank; a familial concentration of the disease in the parents, siblings, and offspring of affected individuals (McKeown, MacMahon, and Record, 1951a,b; McKeown and MacMahon, 1955).

There is another feature of the disease which has lately come to notice (Table I). It has been shown that there are more females than males among the sibs of parents of affected children and that, although this disturbance is present among the sibs of both parents of affected girls, it is found only among the mothers' sibs when the affected children are boys (Knox, 1958a). The finding therefore is limited to sibships from which the affected children drew X-chromosomes. This recalls at once the striking sex ratio of the affected children themselves and suggests that a sex-linked genetic factor may be responsible for both features.

If the situation were indeed so simple that it could be explained in terms of an X-borne recessive gene with equal penetrance of the two appropriate genotypes, then the ratio of females affected to males affected would provide a direct measure of the gene frequency (g). This is because the frequency of the $\dot{X}Y$ genotype in males is g and that of the $\dot{X}\dot{X}$ genotype in females is g^2. Since congenital pyloric stenosis occurs in males and females in the ratio 5:1, the frequency of the hypothetical determining gene would be about 0·2. The immediate implication is that one-fifth of boys and one-twenty-fifth of girls are genetically susceptible to the disease. This amounts to 120 per 1,000 children of both sexes, and since the observed incidence of the disease is about 3 per 1,000 live births the penetrance factor of the appropriate genotypes is about 1/40.

To this extent the hypothesis is entirely consistent with evidence of the importance of non-genetic factors in the aetiology of the disease (McKeown, MacMahon, and Record, 1952). Even if the accuracy of the gene-frequency estimate were upset by unequal penetrance in the two sexes, the incidence of the disease and the evidence of important environmental factors together confirm the general terms of the hypothesis to be tested.

Hypotheses of this nature usually require an apology, for they contain enough variables to fit many different assemblies of data, but in the present case the suggestion is based upon a most remarkable pattern of events whose explanation in other terms has so far proved elusive. The further purpose of this paper is to test the hypothesis by examining its corollaries in relation to the observed facts and to reassess its plausibility in terms of what is found. Many of the corollaries are deduced algebraically and as the deductions are rather complex and the results of more general interest they are the subject of another paper (Knox, 1958b).

Frequency of the Disease in Relatives

(*i*) *Cousins.*—The expected incidence of disease among cousins of children with a disease determined in this manner supplies a basis for a test. With a gene of frequency 0·2 we would not expect a greatly increased total incidence: precisely, 4·4/1,000 cousins against 3/1,000 of the population [Appendix]. Large numbers would be necessary to detect a difference of this degree and it is more relevant to the present purpose that we can expect the proportions of affected maternal and paternal cousins to be, respectively, 0·622 and 0·378.

Data from Birmingham (McKeown and others, 1951b) showed eleven affected among 3,980 cousins of

* Medical Research Council Clinical Research Fellow.

propositi. As anticipated, this fails to distinguish between the population incidence and that expected under the terms of the hypothesis, but eight of the eleven cousins were maternal cousins. I have found seven other papers in which the requisite details of the relationships between affected cousin pairs were given (Cockayne, 1934, 1938; Cockayne and Penrose, 1943; Carter and Savage, 1951; Fenwick, 1953; Carter and Powell, 1954; Nielson, 1954). By counting each affected child in turn as propositus, these authors' papers yield thirty maternal cousins and eighteen paternal ones. Addition to the Birmingham figures makes 41 maternal and 26 paternal compared with expected figures of 41·7 and 25·3 under the terms of the hypothesis. Although the ratio 41/26 does not differ significantly from unity ($\chi^2=3{\cdot}36$; $0{\cdot}05<P<0{\cdot}1$), the theoretical consequences of a sex-linked gene with frequency 0·2 could scarcely correspond more closely with the facts.

(*ii*) *Parents.*—The expected proportion of mothers with genotype $\dot{X}\dot{X}$ is g and the proportion of $\dot{X}Y$ fathers is $2g/(1+g)$ (Knox, 1958b). With a gene of frequency 0·2, we expect a male/female ratio among affected parents of affected children equivalent to 5:3 instead of the population ratio of 5:1. McKeown and MacMahon (1955) reported twelve new families in which the disease occurred in two generations, sometimes with more than one child affected. If each affected child is counted once, these data give nine affected mothers and six fathers. Data supplied by Carter and Powell (1954), treated in a similar manner, give nine mothers and seven fathers. Nielson (1954) reported the families of nine affected parents in which one or more children (eleven altogether) were affected: the necessary information for counting twice the two parents with two affected children was not supplied, but there were three affected mothers and six affected fathers. Nielson also reported a further two affected fathers by tracing his families in the opposite direction. Fenwick (1953) reported a family with a father and two sons affected and a similar family has been reported anonymously (Anon., 1958). Altogether, in these five papers, 46 affected parent-child pairs could be identified and in 25 the affected parent was the father. Under the terms of the hypothesis the expected number is 28·7 and in terms of the population sex ratio it is 38·3. The difference between the latter expectation and the observations is statistically significant, but the facts are quite compatible with the hypothesis of a sex-linked determining gene with frequency 0·2.

However, the available data on parent-child pairs supply the first evidence against the plausibility of an explanation in terms of sex-linkage. McKeown and MacMahon (1955) supply six father-child pairs in which the sex of the child was reported, Carter and Powell (1954) supply seven, Fenwick (1953) two, and the anonymous author (1958) another two. Fourteen of the seventeen children were boys and only three were girls. This differs significantly from the 1:1 ratio expected from a supposed X-recessive gene ($\chi^2=7{\cdot}12$; $P<0{\cdot}01$) and bears a resemblance to the 5:1 population ratio.

(*iii*) *Siblings.*—The available data on affected sib pairs also seem to point against an X-borne recessive gene.

McKeown and others (1951b) found among later sibs of propositi that 12/122 boys and 2/119 girls had the disease. Expected hypothetical $\dot{X}Y$ and $\dot{X}\dot{X}$ genotype frequencies are $(1+g)/2$ boys and g girls (Knox, 1958b). When $g=0{\cdot}2$, the expected sex ratio among affected subsequent sibs of a series of propositi is 3:1 instead of the population ratio of 5:1. The facts do not differ significantly from the expectation for sex-linkage, but resemble the population ratio more closely.

There are no other large-scale systematic studies of the disease in sibs, but a number of other sib-pairs are reported. From nine papers with such information (Brendle, 1937; Donovan, 1938; Adlington, 1943; Cockayne and Penrose, 1943; Shaefer and Erbes, 1948; Todd, 1949; McKeown and others, 1951b; Fenwick, 1953; Anon., 1958) the total of affected sib pairs was 57, distributed as:

MM, 40; MF*, 15; FF, 2.

It can be shown that for an X-recessive gene with equal penetrance in the two sexes the expected ratio MF*/FF is 2:1 at any gene frequency, and that the ratios MM/MF*/FF are $1:2g:g$ (Knox, 1958b). The expected distribution for 57 pairs, for a disease determined by an X-recessive gene frequency 0·2, is:

MM, 35·6; MF*, 14·2; FF, 7·1.

The expected distribution based upon a simple binomial distribution of the population sex ratio is:

MM, 36·5; MF*, 18·2; FF, 2·3.

Larger numbers would be needed to distinguish clearly between the two, and the difference between the observed 15:2 MF*/FF ratio and the expected 2:1 ratio in sex linkage is not significant ($\chi^2=3{\cdot}65$; $0{\cdot}05<P<0{\cdot}1$). But it cannot be denied that the facts correspond more closely with expectations based upon less specific suppositions.

* Irrespective of order, *i.e.* MF+FM

(*iv*) *Relatives as a Whole.*—While the evidence so far presented provides a somewhat paradoxical pattern, one very clear point emerges when the frequencies of disease in different relatives are compared. This is that the full facts of familial concentration cannot be explained in terms of the supposed pattern of inheritance, and that a sex-linkage hypothesis would require considerable supplementation if it were to be comprehensive.

The evidence for this is as follows:

Subject to the possibility of inaccuracy from unequal penetrance in the two sexes, we saw that the frequency of the gene must be about 0·2 and the penetrance about 1/40. It was also shown that the supposed penetrance in cousins appeared to be of the same order. But when the genotype frequencies are considered quantitatively in offspring and siblings the facts require us to suppose much higher levels of penetrance.

McKeown and MacMahon (1955) estimated the incidence of the disease in offspring of propositi to be about 69/1,000. The appropriate hypothetical genotype frequency in offspring of male propositi is g both for boys and girls, and the same factor applies to the daughters of female propositi. All the sons of female propositi are susceptible. Combining these results in correct proportions and substituting $g = 0{\cdot}2$, we expect to find the appropriate genotypes in a little more than a quarter (4/15) of all offspring. Comparison with the observed incidence gives a penetrance factor greater than 1/4, ten times that in the population at large or in cousins.

McKeown and others (1951b) also found an incidence among subsequent sibs of propositi equal to 58/1,000, and the expected frequency of the appropriate genotypes among these sibs is 0·4 (Knox, 1958b). The penetrance factor here is higher than 1/7, again very different from the population and cousin factors.

It is also obvious that inaccuracy of the gene-frequency estimate used in these calculations cannot explain the differences between the high penetrance in offspring and siblings and the much lower penetrance in cousins and in the general population. A lower estimate of g gives an expectation of a distinct difference between the incidence in cousins and in the general population. A higher estimate of g requires that we suppose even wider differences between the penetrance factors in sibs and offspring and in the population.

The similarity between the incidence in cousins and in the population has a more general implication. It limits the degree of genetic specificity which we can legitimately suppose in affected children. Such limitation applies not only to the lower ranges of frequency of a hypothetical sex-linked recessive gene but also to specification in terms of substitutions at more than one locus. This conclusion applies to autosomal as well as sex-linked transmission, and means, in effect, that the main causes of familial concentration are almost certainly non-genetic. It probably applies also to maternal-foetal interactions of the type seen in haemolytic disease of the newborn, because a complete analogy with this disease demands genetic specification of the mother as well as the child. The falling incidence with birth rank, the opposite of the haemolytic disease pattern is also against a simple explanation in this class.

The appeal of the sex-linkage hypothesis therefore is on grounds other than the facts of familial concentration and these facts must be explained in some other way.

Selection and Gene-Frequency Maintenance

The selection and evolutionary aspects of this disease offer some evidence on the plausibility of the sex-linkage hypothesis.

One difficulty in attempting to attribute any common serious disease to a harmful gene is the problem of how a stable gene frequency has been maintained in the face of strong selection. If we suppose that, until recent times genetically speaking, pyloric stenosis was always a fatal disease, there would be a loss of seven hypothetical X-borne harmful genes for every six cases (one $\dot{X}\dot{X}$ and five $\dot{X}Y$). This is the incidence in 2,000 births or 3,000 X-chromosomes. Because we suppose that 4/5 of the 3,000 chromosomes are normal, this represents a loss of seven abnormal per 2,400 normal genes or 1/340 per generation, and if maintenance were by mutation would imply a mutation rate of the same order. This is many times greater than the accepted general level of mutation rates, namely about 1/100,000.

It is in relation to this discrepancy that the phenomenon of a disturbed sex ratio in the parental sibships has particular interest with respect to the possibility that the gene frequency is maintained by female ($X\dot{X}$) heterosis. There are more female sibs than male sibs in each of three groups of parental sibships from which the propositi drew X-chromosomes, but not in the fourth group, the sibships of fathers of affected boys (see Table, opposite).

But, if this is indeed an expression of heterosis, there is reason for surprise at its extent. There were 1,048 aunts and 911 uncles in the three parental

TABLE

UNCLES AND AUNTS OF 445 BOYS AND GIRLS WITH PYLORIC STENOSIS

Sex of Propositus	Paternal		Maternal	
	Uncles	Aunts	Uncles	Aunts
Affected Boys (369)	648 (1·76)	641 (1·74)	683 (1·85)	739 (2·00)
Affected Girls (76)	114 (1·50)	150 (2·00)	114 (1·50)	159 (2·09)
Total 445	762	791	797	898

Mean number per child in parentheses

sibship groups with a disturbed ratio. The genotype frequencies expected among these aunts on the basis of a gene so frequent as 0·2 are:

XX, 0·19; X$\dot{X}$, 0·66; $\dot{X}\dot{X}$, 0·15

compared with population frequencies

XX, 0·64; X$\dot{X}$, 0·32; $\dot{X}\dot{X}$, 0·04

(Knox, 1958b).

By taking the survival value of the genotype XX as 1·0, the value for $\dot{X}\dot{X}$ as 0·975 (1/40 lost), and by presuming that the excess of 1,048 over 911 is entirely due to X$\dot{X}$ heterosis, the survival factor for this last genotype comes to 1·56. If the $\dot{X}\dot{X}$ survival value is less than the arbitrary 0·975, the survival factor for X$\dot{X}$ is higher still, as high as 1·91 when the $\dot{X}\dot{X}$ factor reaches zero. A survival factor of 1·56 for X$\dot{X}$ females applied to the total population results in a gain of about one $\dot{X}$ gene per thirteen normal per generation, many times the loss which could be attributed to the disease itself. It is possible to mitigate some of this imbalance by postulating other losses of $\dot{X}$ genes in the form of unrecognized loss of $\dot{X}\dot{X}$ females, but even with zero survival of $\dot{X}\dot{X}$ (and increase of the X$\dot{X}$ survival factor to 1·91) the expected net gain per generation is still two-thirds of that already given.

The supposition that the sex ratio disturbance in parents' sibs is entirely due to a lethal effect in $\dot{X}$Y males results in equally serious difficulties through aggravating the question of how the gene frequency is maintained.

This results in a situation where we must either accept both hypotheses, loss of $\dot{X}$Y uncles and heterosis in X$\dot{X}$ aunts, or accept neither. While we cannot regard this as a formal *reductio ad absurdum*, there are now a sufficient number of interdependent variables to make the acceptance of neither the natural preference.

This preference is readily supported by an examination of the sex ratios of cousins and later sibs. In these relatives, as in the parents' sibs, we expect frequencies of the X$\dot{X}$ and $\dot{X}$Y genotypes to be higher than in the population (Knox, 1958b). Yet the published data show normal sex ratios (McKeown and others, 1951b). It seems improbable that secular changes sufficient to account for the disappearance of so striking a phenomenon could have occurred in the course of one generation and less likely that parents could have forgotten their male sibs dying relatively late in life on a scale which could explain the difference.

As with the phenomenon of familial concentration of the disease, so with the localization of the disturbed sex ratio in parents' sibs; the causes are to be sought largely or entirely among mechanisms other than sex-linked inheritance.

CONCLUSIONS

The conclusions arising from the above considerations are essentially negative.

The economy of the hypothesis of sex-linkage in explaining both the sex ratio of the disease and the distribution of the disturbed sex ratio in the parents' sibs was supported by the sex ratio observed among affected parents of affected sibs and asymmetry of the attack rates in maternal and paternal cousins. But other features of the disease, including a paucity of FF sib pairs and an unexpected sex ratio among affected children of affected fathers, pointed against this.

The hypothesis was impaired further by the demonstration that it failed to account for all the facts of the familial concentration of the disease and that its validity depended upon finding other means of explaining the greater part of the disparities between the attack rates in parents, sibs, and offspring of propositi, and attack rates in cousins. Such a demonstration cannot serve as formal evidence that there is no genetic determinant, for any genetic hypothesis invoking the concept of limited penetrance must allow the possibility of familial concentrations of environmental factors. But because it is necessary in any case to invoke non-genetic factors in explanation of the facts, it will be accepted that these same facts cannot serve as evidence that genetic factors do exist.

Consideration of selective effects and of gene frequency maintenance added further difficulties to the hypothesis, since it is improbable that the gene could be maintained at a stable level by mutation. Although it seemed at first that the sex ratio disturbance in the parents' sibs might supply a mechanism for such maintenance, critical examination showed that unless a very complex scheme were adopted the disturbance in fact aggravated the problem. Indeed, such difficulties were added that it became difficult to

accept that the disturbance in the parents' sibs could have any simple genetic basis.

The evidence as a whole, therefore, does not permit acceptance of the initial hypothesis. Although it is a negative conclusion the reasoning behind it has been presented in detail because of its importance in the context from which the hypothesis was drawn. A sex-linked genetic explanation of the phenomenon of disturbed ratios among the parents' sibs would have suggested simple genetic explanations for analogous phenomena in other congenital diseases (Knox, 1958b; Stewart, Ferguson-Smith, Lennox and Mack, 1958). Instead, it now seems necessary to replace pyloric stenosis in a class with those other diseases for whose curious ancestor-patterns we likewise have no ready explanation, and to consider other causes.

REFERENCES

Adlington, J. L. (1949). *Brit. med. J.*, **2**, 740.
Anon. (1958). *Ibid.*, **1**, 117.
Brendle, E. (1937). *Mschr. Kinderheilk.*, **68**, 295.
Carter, C. O., and Powell, B. W. (1954). *Lancet*, **1**, 746.
—— and Savage, T. R. (1951). *Arch. Dis. Childh.*, **26**, 50.
Cockayne, E. A. (1934). *Lancet*, **1**, 898.
—— (1938). *Arch. Dis. Childh.*, **13**, 249.
—— and Penrose, L. S. (1943). *Ohio J. Sci.*, **43**, 1.
Donovan, E. J. (1938). *Amer. J. Surg.*, **39**, 377.
Fenwick, T. (1953). *Brit. med. J.*, **2**, 12.
Knox, G. (1958a). (In press).
—— (1958b). *Brit. J. prev. soc. Med.*, **12**, 183
McKeown, T., and MacMahon, B. (1955). *Arch. Dis. Childh.*, **30**, 497.
——, ——, and Record, R. G. (1951a). *Ann. Eugen. (Lond.)*, **16**, 249.
——, ——, —— (1951b). *Ibid.*, **16**, 260.
——, ——, —— (1952). *Arch. Dis. Childh.*, **27**, 386.
Nielsen, O. S. (1954). *Acta paediat. (Uppsala)*, **43**, 522.
Shaefer, A. A., and Erbes, J. (1948). *Surg. Gynec. Obstet.*, **86**, 45.
Stewart, J. S. S., Ferguson-Smith, M. A., Lennox, B., and Mack, W. S. (1958). *Lancet*, **2**, 117.
Todd, R. McLaren (1949). *Brit. med. J.*, **2**, 931.

APPENDIX

EXPECTED FREQUENCY OF GENOTYPES $\dot{X}\dot{X}$ AND $\dot{X}Y$ AMONG COUSINS, SUPPOSING THAT PYLORIC STENOSIS IS CONDITIONALLY DETERMINED BY THESE GENOTYPES

Type of Cousin		Frequencies				
		General		For $g=0{\cdot}2$		
		$\dot{X}Y$	$\dot{X}\dot{X}$	$\dot{X}Y$	$\dot{X}\dot{X}$	$\dot{X}\dot{X}+XY$
Of Maternal	Uncles	g	$g(1+3g)/4$	1/5	2/25	0·140 } 0·2200
	Aunts	$(3+5g)/8$	$g(3+5g)/8$	1/2	1/10	0·300 }
Of Paternal	Uncles	g	$g^2(3+g)/2(1+g)$	1/5	4/75	0·127 } 0·1335
	Aunts	$g(5+3g)/4\ (1+g)$	$g^2(5+3g)/4(1+g)$	7/30	7/150	0·140 }
General Population		g	g^2	1/5	1/25	0·120

The absolute genotype frequencies of 0·2200 and 0·1335 in maternal and paternal cousins are equivalent to proportional frequencies of 0·622 and 0·378. The mean of 0·2200 and 0·1335 is 0·177 compared with a population frequency of 0·120 and gives an expected attack rate in cousins of 4·4 per 1,000 compared with a population attack rate of 3 per 1,000. (See also Knox 1958b.)

Brit. J. prev. soc. Med. (1958), **12**, 193–196

AN ESTIMATE FROM PEDIGREE DATA OF THE GENE FREQUENCY FOR COLOUR BLINDNESS

BY

GEORGE KNOX*

From the Department of Social Medicine, University of Birmingham

There are several possible approaches to the measurement of the population gene-frequency for colour blindness, and each approach has its particular advantages and disadvantages.

The first is the direct approach of a population survey and especially, since the disease is commoner in males, a measurement of its incidence in men. In the event of full penetrance and ascertainment of the XY genotype, the mathematical treatment is commendably simple, for the incidence in men is numerically equal to the gene frequency. The weakness of the method, however, is its dependence upon the presumption of full penetrance and this difficulty is manifest in the varying estimates yielded by different methods at different times. Bell (1933) quotes a survey in 1892 which yielded an estimate of 2·18 per cent. male incidence; Gates (1946) quotes another early survey of 14,846 persons where the male incidence was 4·16 per cent., and other more recent surveys give estimates in European populations of 6·63 per cent. (Grieve, 1946), 7·49 per cent. (Vernon and Straker, 1943), 7·95 per cent. (von Planta, 1928) 8 per cent. (Wright), 8·07 per cent. (Waaler, 1927) 9·7 per cent. (Wieland, 1933), and 10·07 per cent. (Schiötz, 1922). Detection of colour blindness by Ishihara charts is no doubt responsible for recent estimates being higher than earlier ones. But even allowing for this and for the fact that there seem to be geographical variations in the incidence of colour blindness (see Vernon and Straker, 1943), the variations among the different estimates of incidence are sufficient to cause some doubt about the validity of direct conversion of the male incidence to a gene-frequency estimate. Nor indeed would a higher degree of consistency necessarily validate such a conversion; used alone the method does not provide any objective means of assessing its own propensity to over- or under-estimate.

The second approach depends upon the sex ratio of the disease. While the male incidence of a sex-linked disease is proportional to the gene frequency (g), the female incidence is proportional to its square (g^2) (Knox, 1958; Dahlberg, 1947), and provided that the penetrances in the two sexes are equal, though not necessarily complete, the ratio Female affected/Male affected in a population provides an estimate of g. Since the premise upon which this is based is different from the premise of the first method (full penetrance in males) it provides a very useful check. Its disadvantage arises because sex-linked disorders are relatively rare in females and even enormous population surveys yield quite small numbers.

Schiötz (1922) reported an incidence of 10·07 per cent. in 2,005 males and 0·91 per cent. in 2,200 females. The F/M ratio is 0·9, a reasonably close check upon an estimate of g derived from the incidence in males. The 95 per cent. limits for the F/M ratio are 0·052–0·162, wide enough to be compatible with the incidence in males but also wide enough to deprive the estimate of precision.

Waaler (1927) reported an incidence of 8·07 per cent. in 9,047 males and 0·44 per cent. in 9,072 females. Here the F/M ratio is only 0·055, considerably less than the gene-frequency estimate based upon the male incidence. Again, however, the 95 per cent. limits of the ratio are wide, 0·039–0·075, and it is doubtful if the difference between the results of the two methods could be considered statistically significant. But the same remarks apply here as to the data given by Schiötz, the sex ratio seems only to confirm the accuracy of direct estimates in a very general way and in a survey of manageable size can scarcely hope to compete in precision.

A third example of the difficulties of this approach is found in the data of Kilborn and Beh (1934), who found an incidence of 6·5 per cent. in 2,279 male Chinese and 1·7 per cent. in 1,132 females. The sex ratio gives a gene-frequency estimate of 0·26, an inconsistency in the opposite direction to Waaler's and much of it reasonably attributable once more to the small numbers.

A similar inconsistency of greater extent is found in the data of Schmidt (1945), who is reported as finding an incidence of 7 per cent. in males and 4 per cent. in females.

These checks upon direct estimates of the gene frequency for colour blindness generally confirm

* Medical Research Council Clinical Research Fellow.

that it is between about 0·05 and 0·10 in most European populations, but additional data would clearly be welcome. The accurate estimation of the population sex ratio requires large investigations, and I wondered whether legitimate use could be made of existing pedigrees of families with the disorder.

Method

Since the collection of such records is not related to any definable population, a suitable method must depend upon the relative numbers of males and females, and, since selection for publication is based in part upon the number of affected individuals in a family and this in turn is related to the sex ratio, the method should clearly make allowances for such selection. While a precise correction is probably too much to hope for, it seemed possible that one of the algebraic relationships derived from a recent consideration of sex-linked inheritance (Knox, 1958) might supply a sufficiently accurate method. It depends upon the expected frequencies of pairs of affected sibs of the types MM, MF, and FF in the respective relative proportions $1 : 2g : g$, where g is the frequency of a sex-linked recessive gene. An estimate based upon a count of such pairs selects families in much the same way as publication might be expected to do, for it ignores families with less than two affected sibs and it takes greater note of larger sibships, taking $n(n-1)/2$ units of information for a family with n affected sibs (see below). We might therefore expect it to be reasonably robust and relatively resistant to the kind of bias introduced by publication.

The ratios $1 : 2g : g$ were derived originally from the product of the sex ratios of the first of a pair and the expected sex ratio in the next (Knox, 1958). The relationship applies to the sum of all possible pairs when more than two individuals are affected in a sibship, that is, three pairs for three affected, six pairs for four affected, ten pairs for five affected and in general $n(n-1)/2$ for n affected. In order to improve confidence in the contention that all pairs should be counted, an alternative derivation of expected pair frequencies in sibships of size 2 and 3 is presented in the next two panels. These frequencies are based upon successive multiplication of population parental mating-type frequencies, the binomial probabilities of different sex constitutions of the families, and, in each case, the expected genotype frequency combinations. It can be seen that the ratios $1 : 2g : g$ are derived by the addition of the probabilities of all possible pairs of the appropriate types.

It follows from this that the ratio (MF + FF)/MM is $3g$, and that an estimator of g which uses all the information is:

$$\frac{1}{3} \cdot \frac{\mathrm{MF}+\mathrm{FF}}{\mathrm{MM}}.$$

Sibship Size 2
METHOD

Parental Mating Types and Frequencies	Constitution of Family and Frequencies									
	1/4			1/2				1/4		
	MM	*M*M	MM	*MF*	*M*F	M*F*	MF	*FF*	*F*F	FF
$\bar{X}\bar{X}$ $\bar{X}Y$ g^3	1	0	0	1	0	0	0	1	0	0
$X\bar{X}$ $\bar{X}Y$ $2g^2(1-g)$	¼	½	¼	¼	1	0	¼	¼	½	¼
XX $\bar{X}Y$ $g(1-g)^2$	0	0	1	0	0	0	1	0	0	1
$\bar{X}\bar{X}$ XY $g^2(1-g)$	1	0	0	0	0	1	0	0	0	1
$X\bar{X}$ XY $2g(1-g)^2$	¼	½	¼	0	½	0	½	0	0	1
XX XY $(1-g)^3$	0	0	1	0	0	0	1	0	0	1

The cells contain probabilities of 2, 1, 0 affected children for each parental mating type and sex constitution of the family. *M*, *F* indicate affected individuals, $\bar{X}\bar{X}$ or $\bar{X}Y$, and M, F indicate unaffected individuals.

Sibship Size 2

SUMMARY OF SIB-PAIRS

MM	$g(1+g)/8$
MF	$g^2(1+g)/4$
FF	$g^2(1+g)/8$
MM	$g(1-g)/4$
MF	$g(1-g)(2+g)/4$
FF	$g^2(1-g)/4$
FM	$g^2(1-g)/4$
MM	$(1-g)(2-g)/8$
MF	$(1-g)(2-g^2)/4$
FF	$(1-g)(2+2g-g^2)/8$
	1·0

The ratios $MM : MF : FF$ are $1 : 2g : g$.
The ratio $F : M$ is g.

Data and Analysis

The data used for the present estimate are the pedigrees for "Congenital Colour Blindness" published by Bell (1933). There are 185 such pedigrees (Nos. 406 to 590 inclusive). One of these (No. 431) is excluded because it is so atypical and is obviously not a sex-linked recessive transmission. Of the remaining 184 pedigrees, 139 contain at least one affected pair of sibs.

The total numbers of affected sib-pairs, counting all recorded generations and all possible pair-combinations are as follows:

MM	MF	FF
489	71	31

The expected 2:1 MM:FF ratio is very closely realized (see also Csik and Mather, 1937), and the distribution is very different from a binomial distribution.

Sibship Size 3

SUMMARY OF SIBSHIPS AND OF AFFECTED PAIRS

Sipships		Possible Pairs		
		MM	*MF*	*FF*
MMM	$g(1+3g)/32$	$3g(1+3g)/32$	—	—
MMF	$3g^2(1+3g)/32$	$3g^2(1+3g)/32$	$6g^2(1+3g)/32$	—
MFF	$3g^2(1+3g)/32$	—	$6g^2(1+3g)/32$	$3g^2(1+3g)/32$
FFF	$g^2(1+3g)/32$	—	—	$3g^2(1+3g)/32$
MMM	$3g(1-g)/32$	$3g(1-g)/32$	—	—
MMF	$3g(1-g)(2+3g)/32$	$3g(1-g)(2+3g)/32$	—	—
FFF	$3g^2(1-g)/32$	—	—	$3g^2(1-g)/32$
FFM	$3g^2(1-g)/32$	—	—	$3g^2(1-g)/32$
MFM	$3g^2(1-g)/16$	—	$3g^2(1-g)/16$	—
MFF	$3g^2(1-g)/16$	—	$3g^2(1-g)/16$	—
MMM	$3g(1-g)/32$	—	—	—
MMF	$3g(1-g)(2-g)/16$	—	—	—
MFF	$3g(1-g)(4+g)/32$	—	—	—
FFF	$3g^2(1-g)/32$	—	—	—
FFM	$3g^2(1-g)/16$	—	—	—
FMM	$3g^2(1-g)/32$	—	—	—
MMM	$(1-g)(4-3g)/32$	—	—	—
MMF	$3(1-g)(4-2g-g^2)/32$	—	—	—
MFF	$3(1-g)(4-3g^2)/32$	—	—	—
FFF	$(1-g)(4+4g-3g^2)/32$	—	—	—
	1·0	$3g(1+g)/8$	$3g^2(1+g)/4$	$3g^2(1+g)/8$
		1 :	$2g$:	g

Numbers of affected males and females in the 184 families are 845 and 93, some individuals being counted several times in the pair-combinations and others not at all.

The sex ratio is therefore 0·11, but reasons have been given for supposing that this is not a legitimate estimate of g in the present circumstances. On the other hand the method based on the MM : MF : FF ratios and proposed above as a legitimate one gives:

$$g = \frac{1}{3} \cdot \frac{MF+FF}{MM} = \frac{1}{3} \cdot \frac{102}{489} = 0{\cdot}070\,.$$

The 95 per cent. limits for this estimate (i.e. based on the ratio 102 : 489) are 0·056–0·086.

Conclusions

The precision of this result is higher than for the estimates based upon the sex ratio in populations, and in magnitude it corresponds closely with most of the estimates based upon male incidence as measured by Ishihara testing. This close correspondence is noteworthy from several points of view.

First, it is an endorsement of Ishihara testing as an accurate means of detecting colour blindness. Secondly, it confirms the validity of the concept of a sex-linked recessive gene as the main determinant of the defect. Alternatively, since the present result is manifestly sensible in relation to others, it can be regarded as an endorsement of the method used.

Summary

Gene-frequency estimates for colour blindness have been obtained by two main methods, the first depending upon the incidence of the defect in males, the other upon the sex ratio. The methods depend on different premises and provide a useful mutual check but the second method can give precise results only in enormous surveys. A new method is suggested based upon published pedigree data. It is found to give a relatively precise result and the estimate of 0·07 corresponds closely with those of direct methods.

References

Bell, J (1933). "Treasury of Human Inheritance", vol. 2. University Press, Cambridge.
Csik, J., and Mathur, K. (1937). *Ann. Eugen. (Lond.)*, **8**, 126.
Dahlberg, G. (1947). "Mathematical Methods for Population Genetics". Karger, Basel.
Gates, R. R. (1946). "Human Genetics", vol. 1. Macmillan, New York.
Grieve, H. (1946). *Nature (Lond.)*, **157**, 376.
Kilborn, L. G., and Beh, Y. T. (1934). *Science*, **79**, 34.
Knox, G. (1958). *Brit. J. prev. soc. Med.*, **12**, 183
Planta, P. von (1928). *v. Graefes Arch. Ophthal.*, **120**, 253.
Schiötz, I. (1922). *Klin. Mbl. Augenheilk.*, **68**, 498.
Schmidt, I. (1945). Unpublished data.
Vernon, P. E., and Straker, A. (1943). *Nature (Lond.)*, **152**, 690.
Waaler, G. H. M. (1927). *Z. indukt. Abstamm. u. VerebLehre*, **45**, 279 (*cited by* Gates, 1946, p. 154).
Wieland, M. (1933). *v. Graefes Arch. Ophthal.*, **130**, 441.
Wright, W. D. (1944). "The Measurement of Colour", p. 52. Hilger. London.

Brit. J. prev. soc. Med. (1958), **12**, 197–203

SEASONAL SWING IN MORTALITY IN ENGLAND AND WALES

BY

ATH. P. KANELLAKIS

Department of Bacteriology and Immunology, Athens School of Hygiene

The very detailed tables of deaths in England and Wales which are published annually by the Registrar-General permit a close examination of the variation in mortality that occurs month by month. It can be studied separately for each sex, at different ages, and for the numerically important causes of death. For the purpose of the present study the deaths that took place in each month in the 5 years 1952–56 were added together. They were then adjusted to allow for the varying length of the calendar month and expressed as a percentage of the deaths occurring throughout the whole 5 years. The variability of these percentages has been measured by the coefficient of variation. This variability, together with the months of maximum and minimum mortality, and the ratios of one to the other, is set out by age and sex in Table I. The monthly changes are shown in more detail in Fig. 1 A and B (overleaf).

VARIABILITY BY AGE AND SEX.—The seasonal swing is least marked, it will be seen, in the neo-natal period of life. At these early ages, congenital defects, birth injuries, and prematurity form the dominating causes of death and the external environment is likely to be of relatively little importance. There is, however, a sharp change in the remaining period of the first year of life. In these 11 months of age the seasonal variability is at its maximum with a coefficient of variation of 34. The coefficient then falls steadily with age until, at 55 years and above, the population reveals once more an increasing susceptibility to the winter environment and its attendant respiratory infections. The seasonal variability in the very old (75 and over) approaches that in the very young.

With one exception the sexes behave alike. The exception lies in the age group 5–14 years where the monthly variation is appreciably higher for the boy than for the girl (19 to 13 per cent.), and the month of maximum mortality for the male (August), unlike that for the female (February), is quite out of keeping with the remainder of the Table. This is the only distribution with a summer maximum. The published data do not allow the causes of death to be examined within the age groups, but there seems little doubt that accidental drowning underlies this striking age and sex disparity. The boys aged 5–14 had a greater annual death rate in 1952–56 than girls of the same age, and this excess was due mainly to deaths from violence. They had almost $2\frac{1}{2}$ times as many deaths from accidents, and seven times as many boys were accidentally drowned—760

TABLE I

PERCENTAGE MONTHLY DISTRIBUTION OF DEATHS FROM ALL CAUSES, BY AGE. ENGLAND AND WALES, 1952–56

Age	Coefficient of Variation		Month of				Ratio of Maximum to Minimum No. of Deaths	
			Maximum		Minimum			
	Males	Females	Males	Females	Males	Females	Males	Females
Under 4 wks	8	9	Feb.	Feb.	Aug.	Sept.	1·3	1·3
4 wks–1 yr	34	34	Feb.	Jan.	Aug.	Aug.	2·6	2·5
1 yr	23	23	Jan.	Feb.	Sept.	July	2·1	1·9
2–4	12	16	Feb.	Feb.	Oct.	Aug.	1·5	1·6
5–14	19	13	Aug.	Feb.	Oct.	Sept.	1·5	1·5
15–54	11	12	Feb.	Feb.	Sept.	July	1·4	1·4
55–74	20	18	Feb.	Feb.	Aug.	Aug.	1·8	1·7
75 and Over	26	26	Feb.	Feb.	Aug.	Aug.	2·1	2·1
All Ages	20	21	Feb.	Feb.	Aug.	Aug.	1·8	1·8

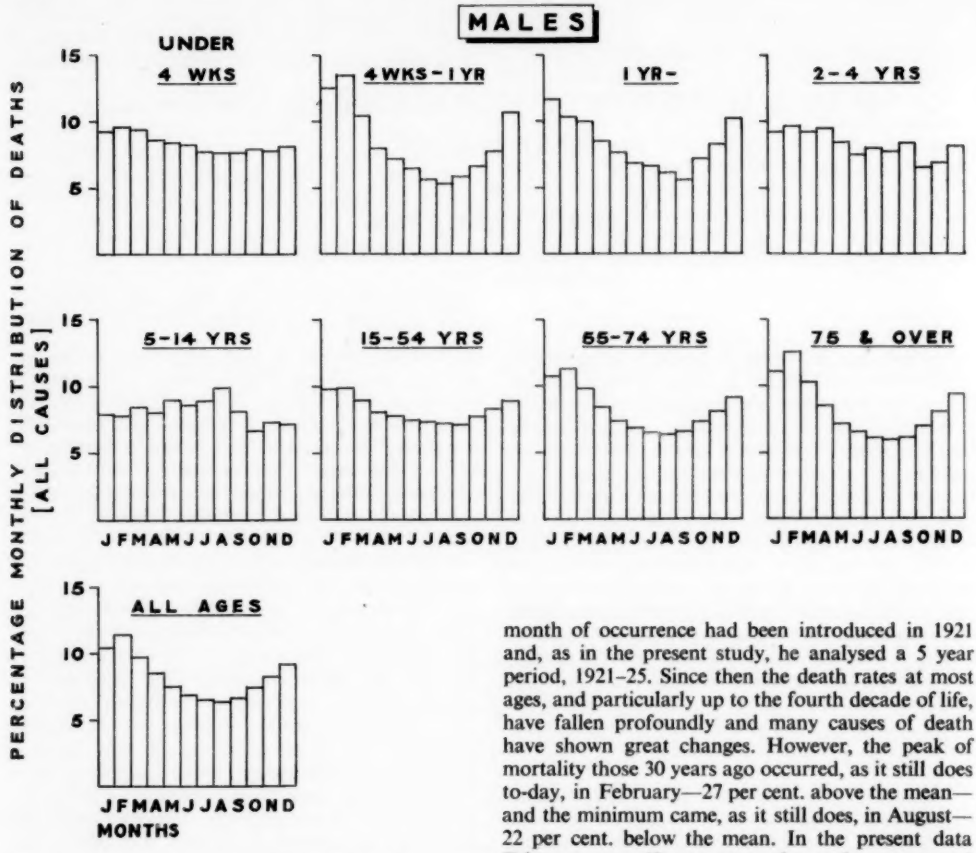


FIG. 1A.—Percentage monthly distribution of male deaths from all causes, by age. England and Wales, 1952–56.

compared with only 108 girls. The curve for girls does show some rise in the number of deaths in July and August (Fig. 1B), but the change is far less pronounced than for boys.

With this exception the predominating month for the peak of mortality in England and Wales is February. The minimum is less consistent. At all ages the rate falls in August for both sexes, but at different ages it varies from July to October. As would be expected on the large numbers concerned, the χ^2 test shows a significant departure from linearity for each age group for each sex.

The seasonal movement at all ages can be compared with that reported by the Registrar-General in his annual report for 1925. His table of deaths by month of occurrence had been introduced in 1921 and, as in the present study, he analysed a 5 year period, 1921–25. Since then the death rates at most ages, and particularly up to the fourth decade of life, have fallen profoundly and many causes of death have shown great changes. However, the peak of mortality those 30 years ago occurred, as it still does to-day, in February—27 per cent. above the mean—and the minimum came, as it still does, in August—22 per cent. below the mean. In the present data February was 40 per cent. above the mean and August still 22 per cent. below. The increase in the winter peak is due, one would suggest, to the ageing of the population and to the greater susceptibility to winter conditions which is shown by the old (see Table I).

The monthly distributions in 1921–25 and in 1952–56 are set out in detail in Table II (opposite).

In spite of the changing picture in national mortality referred to above, the distributions are remarkably similar. No comparisons by age can be made, however, since this feature was not introduced into the tabulation until a much later date.

VARIABILITY BY CAUSE OF DEATH.—Corresponding figures for various causes of death are given in Table III (overleaf) and are shown in more detail in Fig. 2 A and B (overleaf).

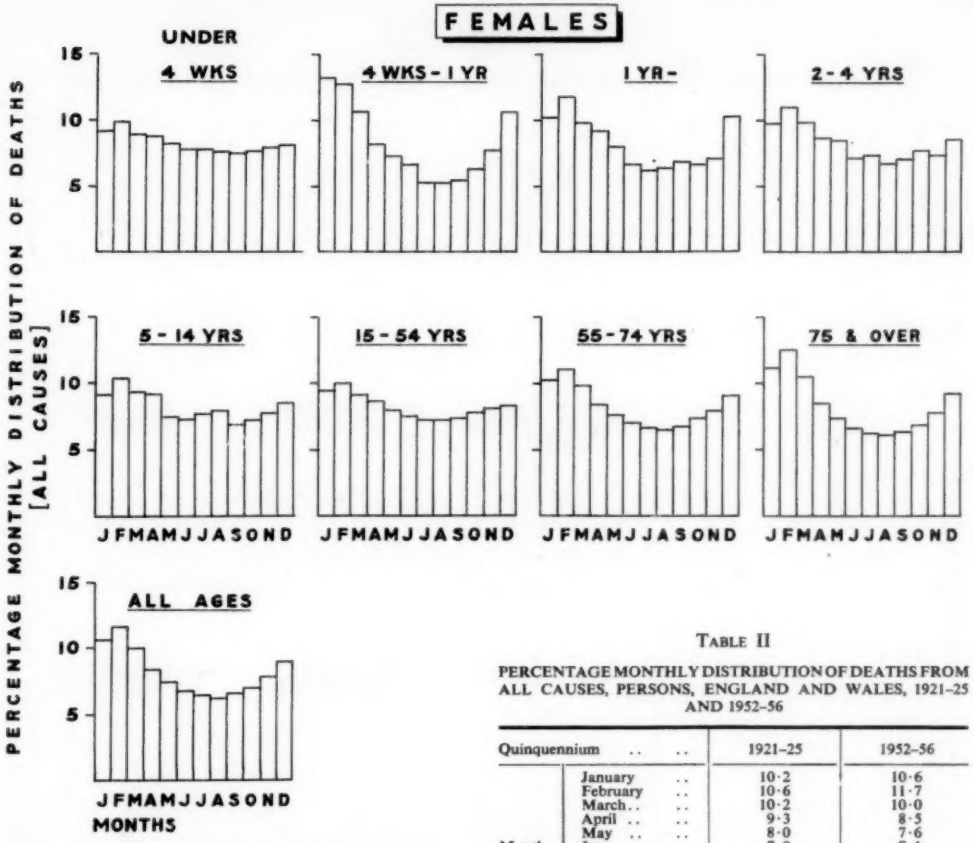


FIG. 1B.—Percentage monthly distribution of female deaths from all causes, by age. England and Wales, 1952–56.

As would be anticipated, the greatest seasonal variation is a feature of the respiratory illnesses—influenza, pneumonia, bronchitis, asthma, and bronchiectasis.

At a lower level, quite considerable variation is shown by diseases of the heart and circulation and by diseases of the digestive system. On the other hand, there is very little variation in the month of dying with the important cancers of the lung and stomach. The maximum number of deaths from all these various causes falls mainly in February. One striking exception for both sexes lies in suicide. Here the curve rises to a peak in April. The minimum is distinctly more variable in its appearance and reveals one or two curiosities; *e.g.* deaths from appendicitis are at their lowest point in November for males and in December for females, and cancer deaths in both sexes touch their lowest point in the spring. The only sex difference of any magnitude appears to lie in accidental deaths, where at all ages the male monthly proportion is more uniform than the female.

On the χ^2 test there was a significant departure from linearity for all causes except cancer of the stomach, appendicitis, and diseases of the liver and gall bladder, but though technically significant the deviations for many other causes were quite small.

TABLE II

PERCENTAGE MONTHLY DISTRIBUTION OF DEATHS FROM ALL CAUSES, PERSONS, ENGLAND AND WALES, 1921–25 AND 1952–56

Quinquennium		1921–25	1952–56
Month	January	10·2	10·6
	February	10·6	11·7
	March	10·2	10·0
	April	9·3	8·5
	May	8·0	7·6
	June	7·0	7·1
	July	6·6	6·6
	August	6·5	6·5
	September	6·7	6·7
	October	7·0	7·3
	November	8·4	8·1
	December	9·5	9·3
Total		100·0	100·0

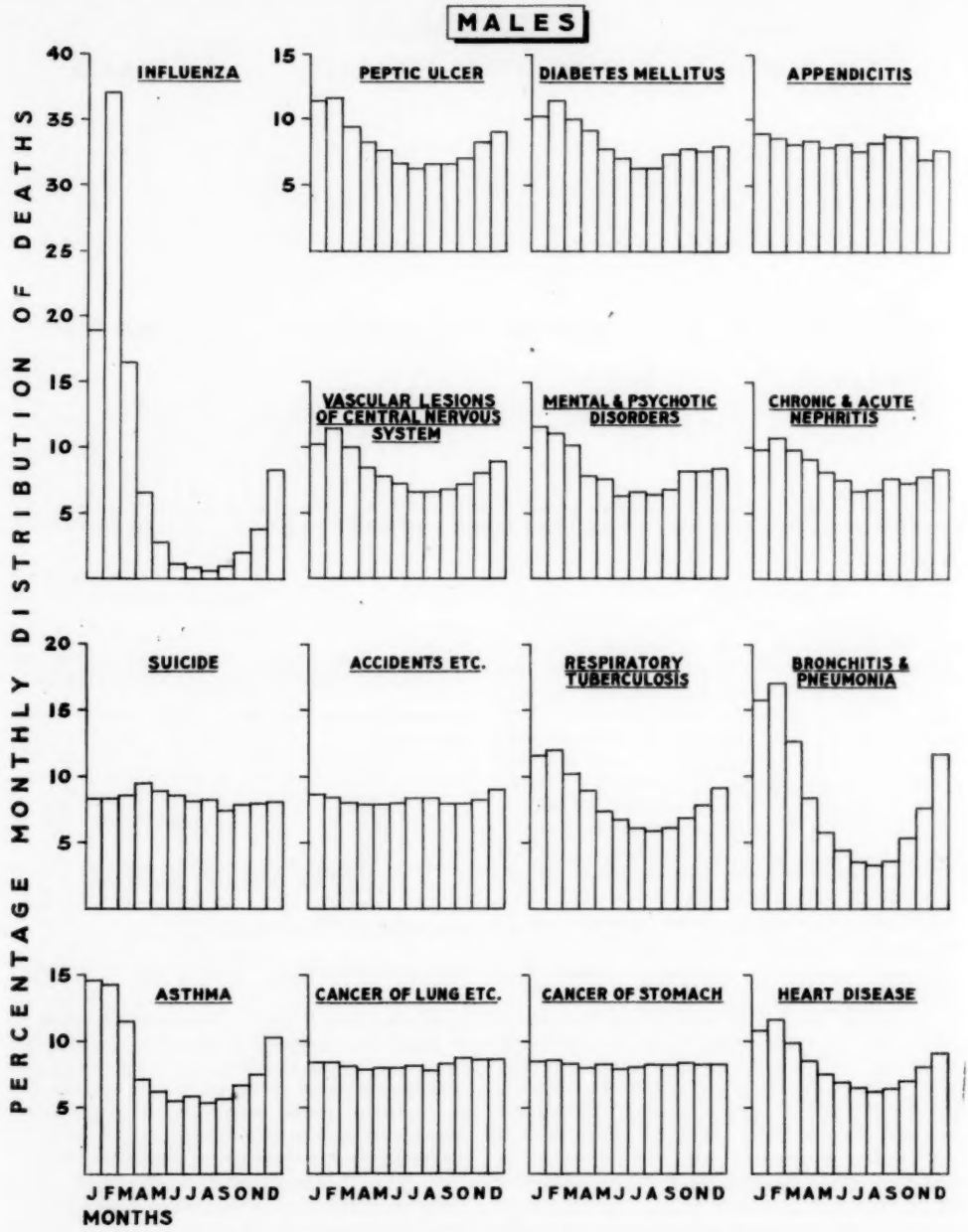


FIG. 2A.—Percentage monthly distribution of male deaths by cause. England and Wales, 1952–56.

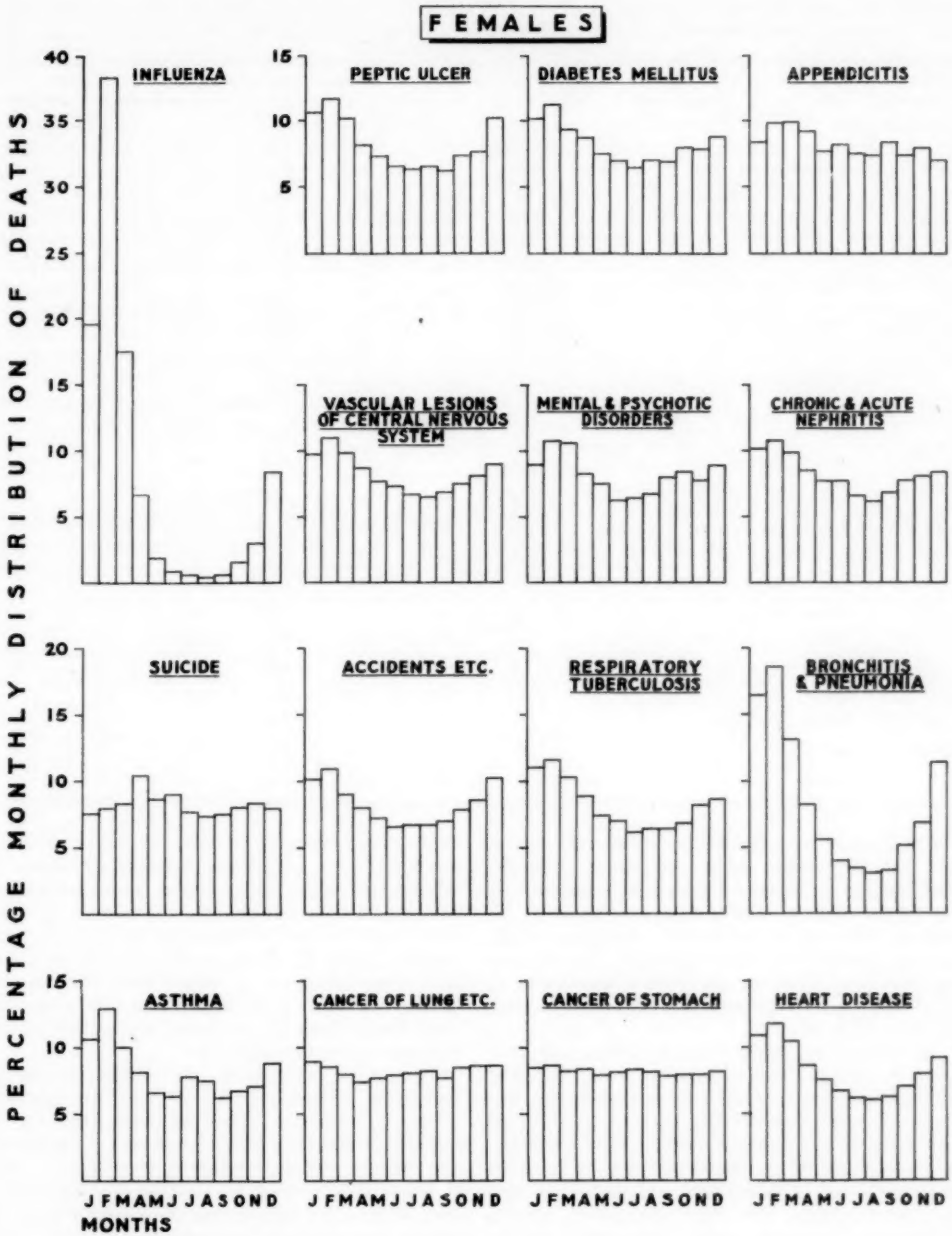


FIG. 2B.—Percentage monthly distribution of female deaths by cause. England and Wales, 1952–56.

TABLE III

PERCENTAGE MONTHLY DISTRIBUTION OF DEATHS BY CAUSE
ENGLAND AND WALES, 1952–56

International List No.	Cause of Death	Coefficient of Variation		Month of				Ratio of Maximum to Minimum Deaths	
				Maximum		Minimum			
		Males	Females	Males	Females	Males	Females	Males	Females
480–483	Influenza	132	138	Feb.	Feb.	Aug.	Aug.	62·0	76·6
490–502	Bronchitis and Pneumonia	59	65	Feb.	Feb.	Aug.	Aug.	4·9	5·9
526	Bronchiectasis	42	44	Feb.	Feb.	July	July	3·4	4·0
241	Asthma	42	25	Jan.	Feb.	Aug.	Sept.	2·7	2·1
001–008	Tuberculosis of the Respiratory System	26	23	Feb.	Feb.	Aug.	July	2·1	1·9
420–434	Diseases of the Heart	21	24	Feb.	Feb.	Aug.	Aug.	1·9	2·0
440–447	Hypertensive Disease	22	23	Feb.	Feb.	Aug.	Aug.	1·9	2·0
290–299	Diseases of the Blood and Blood-forming Organs	10	10	Jan.	Feb.	Nov.	July	1·4	1·3
330–334	Vascular Lesions affecting the Central Nervous System	18	17	Feb.	Feb.	Aug.	Aug.	1·7	1·7
450	General Arteriosclerosis	25	24	Feb.	Feb.	Aug.	Aug.	2·1	1·9
300–326	Mental, Psychoneurotic, and Personality Disorders	22	19	Jan.	Feb.	June	June	1·9	1·7
550–553	Appendicitis	7	11	Jan.	March	Nov.	Dec.	1·3	1·4
540–542	Peptic Ulcer	22	22	Feb.	Feb.	July	Sept.	1·8	1·8
590–594	Nephritis, Acute and Chronic	15	17	Feb.	Feb.	July	Aug.	1·6	1·7
260	Diabetes Mellitus	6	17	Feb.	Feb.	Aug.	July	1·8	1·7
151	Cancer of the Stomach	2	3	Feb.	Feb.	June	May	1·1	1·1
162–165	Cancer of the Lung	4	6	Feb.	Jan.	April	April	1·1	1·2
E970–E979	Suicide	7	10	April	April	Sept.	Aug.	1·3	1·4
E800–E965	Accidents and Violence	5	17	Dec.	Feb.	April	June	1·2	1·6
794	Senility	32	25	Feb.	Feb.	Aug.	Sept.	2·4	2·0
	All Causes	20	21	Feb.	Feb.	Aug.	Aug.	1·8	1·8

Comparison with the Registrar-General's figures for 1921–25 reveals some interesting contrasts. The first lies in the very considerable attention that he rightly pays to deaths from the common infectious diseases of childhood—whooping cough, measles, scarlet fever, and diphtheria. To-day none of them is of sufficient quantitative importance to call for any special attention, and they do not appear at all in Table III.

In 1921–25, no cause of death showed such variation as influenza and to-day that is still true. The ratio of maximum to minimum a generation ago, was however, very distinctly less than to-day—21-fold compared with the figure of 60 to 70 in Table III. The earlier period contained two sharply epidemic years, 1922 and 1924, and these have had no parallel in recent times. The main respiratory causes, bronchitis, pneumonia, and asthma, show no appreciable change in their seasonal swing between 1921–25 and the present time. On the other hand mortality from respiratory tuberculosis shows a significantly wider swing to-day than previously. The Registrar-General shows a maximum in February which is only 1·4 times its minimum in September. Table III shows a ratio as high as 2 for both sexes combined. It would seem that, as the disease is brought under control, the deaths become more concentrated in the period of least favourable environmental circumstances.

One point to which the Registrar-General repeatedly turned in 1921–25 was the possible effects of Christmas upon the death rate. For a number of causes of death he records a December elevation in mortality followed by a January depression. This he noted, for example, with diabetes—and "at no other time of year can the temptation to dietetic and other indiscretions be so great"; this he observed with heart disease (particularly that

associated with the coronary artery)—and "Christmas is, of course, a season of excitement and overindulgence in food and drink when even sufferers from recognized heart disease may be tempted by the spirit of good fellowship into taking undue risks"; and this he also observed with aneurysm and arteriosclerosis and the peptic ulcers. Whatever the explanation—whether it is that our diseases or our habits are to-day more restrained—none of these December elevations appears in the figures for 1952–56. Fig. 2 reveals no such rise in December with a subsequent fall in January. The phenomenon has disappeared.

Finally the tendency to take one's own life in 1921–25 showed a high level through April, May, and June with a slight peak in the final month. In 1952–56 the peak falls earlier, in April, but the variation over the whole year is, compared with all causes of death, relatively small—and was equally so in 1921–25.

Summary

The seasonal variability of mortality in England and Wales has been examined for the years 1952–56. The greatest variability is found at the extremes of life, in the age groups 4 weeks to 1 year and 75 years and over. The predominating peak month of mortality is February, with the month of minimum varying between July and October. Most causes of death show some degree of variation, the swing being greatest with the respiratory infections and least with cancer. Two striking exceptions to the general trend are a peak mortality for boys aged 5–14 years in August, which is due, almost certainly, to accidental drownings, and a relatively high level of suicides in the spring. There is in these modern figures no sign of the December rise in mortality from such diseases as diabetes, heart disease, and peptic ulcers, which was noted by the Registrar-General in the corresponding figures for 1921–25, and which, he suggested, was due to the excitements and indiscretions of Christmas.

I acknowledge my gratitude to Dr. W. J. Martin for much help and advice in the analysis of these figures and to Professor Bradford Hill, in whose Department at the London School of Hygiene and Tropical Medicine, and at whose suggestion, the study was undertaken during my tenure of a Fellowship awarded by the World Health Organization.

Brit. J. prev. soc. Med. (1958), **12**, 204–209

ARTERIAL BLOOD PRESSURE IN PLANTATION WORKERS IN NORTH-EAST INDIA

BY

J. M. G. WILSON

London

The arterial blood pressure in Asiatic and African peoples is usually reported as being lower than that in the western world, (Cadbury, 1922; Kilborn, 1926; Tung, 1930; Chopra, Chopra, and Chopra, 1942; Munro, 1949; Bibile, Cullumbine, Kirtisinghe, Watson, and Wirkramanyake, 1949; Williams, 1941; Alam and Smirk, 1943), and also as being lower in Caucasians living in Asia than when at home (Foster, 1927; Tung, 1927). The rise of blood pressure with age, particularly in the female, found in Britain (Hamilton, Pickering, Roberts, and Sowry, 1954) and the U.S.A. (Master, Dublin, and Marks, 1950) appears not to have been noted, except by Chopra and others (1942) in India, and by Ordman (1948), who observed a moderate rise with age in men in South Africa. Other age-specific records show either no rise at all, or only a very slight one, with advancing years. These East-West differences are variously ascribed to inherent racial distinctions, or to such environmental factors as diet, climate,

TABLE I

MEAN ARTERIAL BLOOD PRESSURES OF ASSAM LABOUR FORCE, WINTER (JANUARY–FEBRUARY, 1956) (3,377 SUBJECTS)

Age (yrs)	Females						Males					
	Systolic			Diastolic			Systolic			Diastolic		
	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
10–14	33	110·0	10·9	32	62·8	8·0	30	103·5	9·5	30	59·6	6·0
15–19	218	114·8	11·9	214	67·3	9·0	160	113·2	9·6	160	65·4	7·3
20–24	289	116·3	10·4	287	69·7	9·7	182	116·3	11·3	181	68·1	9·2
25–29	275	117·2	14·1	273	72·1	10·0	279	117·8	10·7	273	70·8	8·1
30–34	215	118·5	16·0	215	72·9	9·7	254	119·0	11·9	256	72·7	8·9
35–39	199	124·2	10·1	199	76·5	9·8	248	121·0	13·6	249	74·2	9·2
40–44	151	127·6	21·7	150	79·6	12·2	197	125·0	17·1	194	76·0	9·2
45–49	95	136·3	25·2	92	83·5	12·8	161	127·0	17·7	160	78·3	10·0
50–54	47	139·8	20·8	47	85·4	11·7	121	132·0	23·6	118	81·4	11·7
55–59	43	147·0	23·8	44	88·5	14·1	74	144·3	27·4	75	83·0	11·3
60–64	24	155·2	22·5	23	92·9	12·5	43	144·3	26·2	43	83·7	14·3
65–69	13	151·7	29·5	13	90·5	12·2	18	161·1	25·3	20	88·1	8·8
70–74	2	174·5	56·0	2	88·5	9·9	6	162·5	18·8	6	91·2	9·9
Total Subjects	1,604*			1,591*			1,773*			1,765*		

* In some cases the systolic and diastolic pressures could not be satisfactorily recorded.

TABLE II

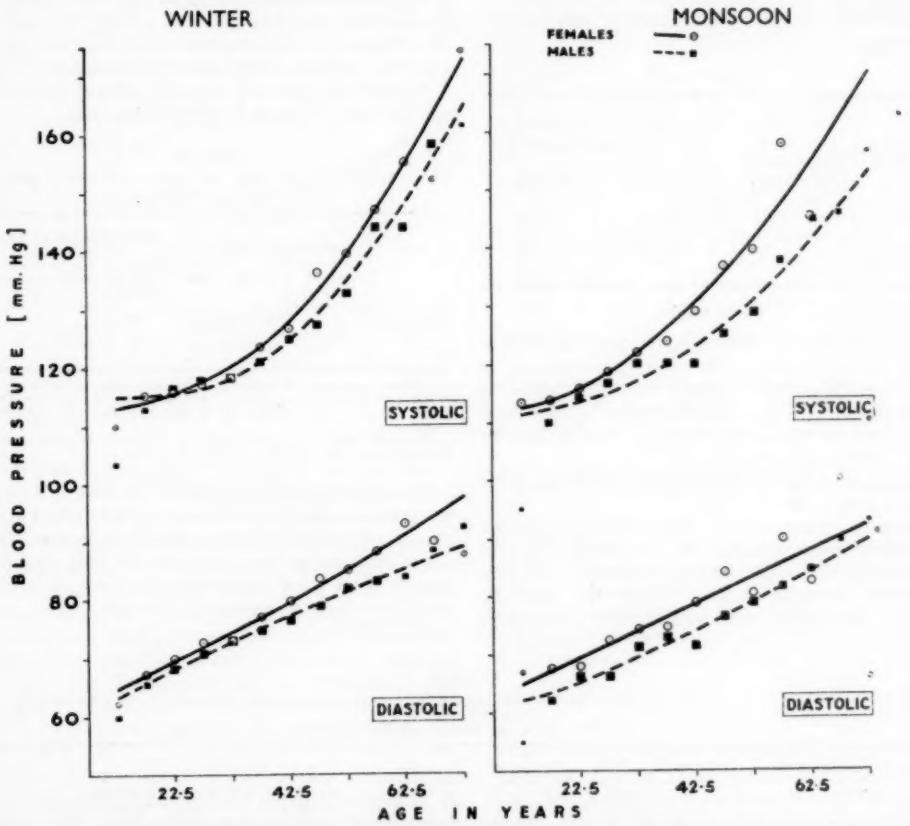
MEAN ARTERIAL BLOOD PRESSURES OF ASSAM LABOUR FORCE, MONSOON (JULY–SEPTEMBER, 1956) (1,711 SUBJECTS)

Age (yrs)	Females						Males					
	Systolic			Diastolic			Systolic			Diastolic		
	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
10–14	10	112·9	11·3	10	66·9	9·7	2	94·5	—	2	54·5	4·0
15–19	155	113·5	10·6	156	67·4	8·8	107	110·0	9·3	106	63·5	8·6
20–24	108	115·9	10·1	107	68·0	9·2	98	114·8	10·4	98	66·8	7·9
25–29	115	119·1	14·2	116	72·2	9·5	97	116·2	10·6	96	67·1	9·4
30–34	129	121·4	13·9	128	74·1	9·0	152	119·8	16·4	152	71·4	9·5
35–39	67	123·3	21·7	66	74·5	10·6	106	119·9	15·5	103	72·6	9·5
40–44	88	129·0	22·2	88	78·5	11·0	97	120·0	15·0	97	71·8	9·6
45–49	64	136·5	24·5	64	83·3	12·6	88	125·4	17·7	88	76·5	11·1
50–54	33	139·1	26·2	32	80·5	12·6	61	128·6	11·8	61	79·1	12·1
55–59	23	157·5	30·7	23	89·5	10·2	46	137·5	25·0	48	81·5	11·4
60–64	16	144·5	24·1	16	83·5	11·8	32	144·3	33·1	31	84·3	14·8
65–69	3	182·5	23·5	3	99·8	15·2	9	146·0	24·0	9	89·2	14·4
70–74	1	110·5	—	1	67·5	—	4	156·5	30·2	4	92·5	11·7
Total Subjects	812			810			899			895		

physical activity, and health, and to variations in the degree of mental strain encountered in daily life. The operation of such factors is hard to prove and the various methods of recording and reporting results make comparisons difficult.

It is of interest, therefore, to set on record the age- and sex-specific arterial blood pressures found in an Indian population of Upper Assam tea-garden labourers. The blood pressures were recorded with clinical mercury sphygmomanometers, with a cuff width of 13 cm., at the end of a short routine physical examination at which the subject was recumbent. No people known to be ill were included. Examinations were carried out by the Indian doctors in charge at twelve hospitals within the group of gardens served by the writer. The technique and the manometers used were personally checked and there was reasonable agreement between random readings taken in collaboration with the doctor directly responsible for the examinations. The diastolic blood pressure was taken as the point of disappearance of the Korotkoff sounds. The first sample of the population was examined in the winter season, (Table I, Fig.1). The second and similar sample (a continuation of the same series of physical examinations; selection was made by place of residence on the garden and was considered unlikely to have any bearing on the results) was examined in the monsoon season (Table II, Fig. 2).

The equations on which the curves in Figs 1 and 2



FIGS 1 and 2.—Mean systolic and diastolic arterial blood pressure of men and women tea-garden labourers in Assam, showing growth of pressure with age. Females—Continuous line and open circles. Males—Broken line and squares.

Note: In this and other figures the size of each square or circle has been varied to correspond with the number of observations in each age group. All curves are fitted quadratics (see text).

TABLE III

QUADRATIC EQUATIONS FOR FITTED CURVES BY AGE AND SEX OF ARTERIAL BLOOD PRESSURE IN ASSAM TEA GARDEN LABOURERS—WINTER AND MONSOON

Season	Sex	Blood Pressure	Equation
Winter (January–February, 1956)	Male	Systolic	$y = 119{\cdot}4900 - 0{\cdot}5632x + 0{\cdot}01619x^2$
		Diastolic	$y = 57{\cdot}0032 + 0{\cdot}49992x + 0{\cdot}000928x^2$
	Female	Systolic	$y = 116{\cdot}59 - 0{\cdot}43408x + 0{\cdot}016768x^2$
		Diastolic	$y = 59{\cdot}5883 + 0{\cdot}3916x + 0{\cdot}001776x^2$
Monsoon (July–September, 1956)	Male	Systolic	$y = 111{\cdot}9922 - 0{\cdot}16368x + 0{\cdot}010016x^2$
		Diastolic	$y = 58{\cdot}9823 + 0{\cdot}25584x + 0{\cdot}00232x^2$
	Female	Systolic	$y = 111{\cdot}1508 - 0{\cdot}06752x + 0{\cdot}011968x^2$
		Diastolic	$y = 58{\cdot}8377 + 0{\cdot}46816x - 0{\cdot}00008x^2$

Where y = arterial blood pressure in mm. Hg; x = age in completed years

Records of birth are not available for the older people and an estimate of age has been based on a combination consisting of the doctor's personal knowledge of the subject and of the result of his physical examination.

are based are shown in Table III.

The mean monthly temperatures and rainfall are shown in Table IV.

TABLE IV

Season 1956	Mean Monthly Rainfall (in.)	Mean Monthly Atmospheric Temperature (°F.)	
		Maximum	Minimum
Winter	1·82	74·0	49·6
Monsoon	9·76	88·9	74·5

DISCUSSION

The first point of interest is that systolic and diastolic blood pressures rise with age, more so in females than in men, in much the same fashion as that followed by the sample examined by Hamilton and others (1954), using similar criteria in London (Figs 3 and 4 opposite).

The curves for the London series are based on the equations in Table V.

Secondly, there is very little difference between the blood pressure levels, at comparable ages, of the Indian and the Londoner, despite a marked difference in bodily habitus (Table VI), diet, and physical and mental environment. When allowance is made for differences in mean arm size* (Pickering, Roberts, and Sowry, 1954). (Table VI), and in the criterion for measurement of the diastolic blood pressure (muffling rather than disappearance of the Korotkoff sounds), such variation as there is between the two sets of curves is further minimized.

TABLE VI

MEAN WEIGHT AND ARM SIZE (ALL AGES) OF A SERIES OF INDIAN SUBJECTS

Sex	Mean Body Weight*		Mean Mid-Biceps Arm Circumference	
	No. of Subjects	Weight (kg.)	No. of Subjects	Circumference (cm.)
Male	42	45·6 (100 lb.)	566	22·8
Female	72	37·7 (83 lb.)	531	21·2

* These weights are the mean of a small series selected for admission to hospital for investigation of renal function, in part a random sample of the entire sample and in part patients with high blood pressure.

The mean weight of 1,977 males of the blood pressure sample population was 44·3 kg. S.D. 4·9 (97·5 lb. S.D. 10·7).

Thirdly, when the mean blood pressure in a similar sample under nearly identical conditions, except climatic, is compared, there appears to be very little variation between the curves for the cold and hot season (Figs 5 and 6, overleaf).

* See Appendix.

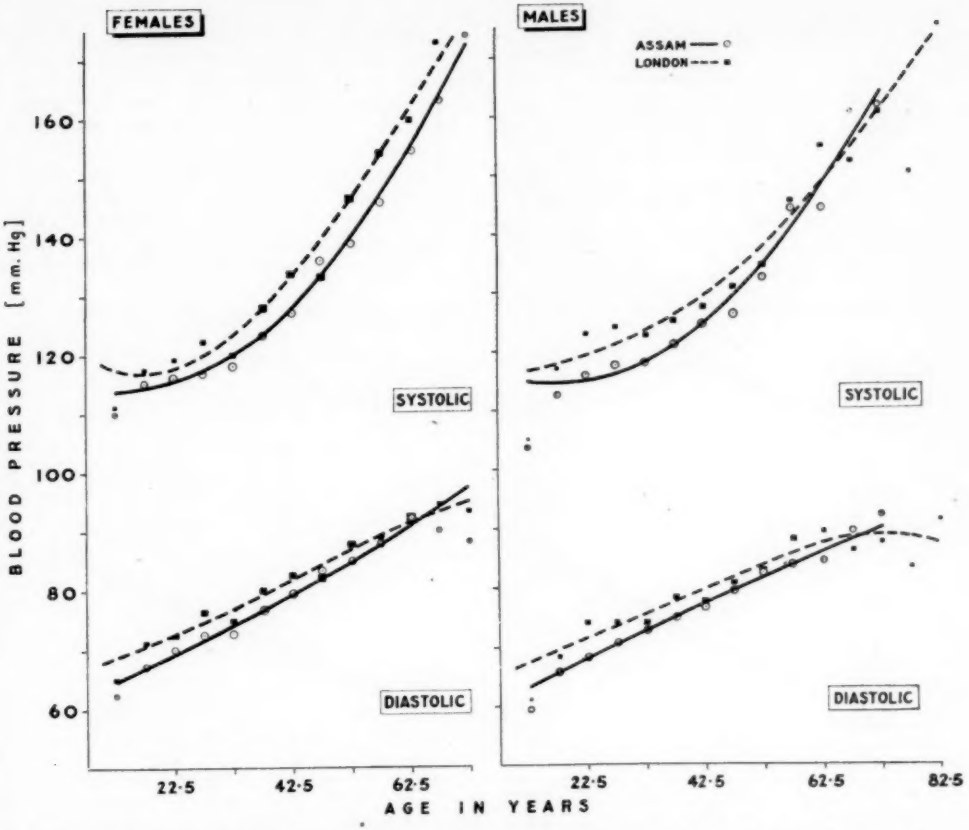
TABLE V

EQUATIONS FOR CURVES OF ARTERIAL BLOOD PRESSURE BY AGE FOR ST. MARY'S HOSPITAL OUT-PATIENTS (FIGS 3 AND 4)

Hamilton, Pickering, Roberts, and Sowry (1954)

Blood Pressure	Sex	Equation
Systolic	Female	$y = 126{\cdot}22 - 1{\cdot}139x + 0{\cdot}037977x^2 - 0{\cdot}00017339x^3$
	Male	$y = 115{\cdot}20 + 0{\cdot}084048x + 0{\cdot}0035098x^2 + 0{\cdot}000057291x^3$
Diastolic	Female	$y = 66{\cdot}74 + 0{\cdot}033445x + 0{\cdot}011264x^2 - 0{\cdot}000087369x^3$
	Male	$y = 62{\cdot}67 + 0{\cdot}32862x + 0{\cdot}0030821x^2 - 0{\cdot}000038879x^3$

Where y = arterial pressure in mm. Hg; x = age in completed years



FIGS 3 and 4.—Mean systolic and diastolic arterial blood pressure of men and women tea-garden labourers in Assam, showing rise in pressure with age, compared with similar curves obtained at St. Mary's Hospital, London by Hamilton, Pickering, and Sowry (1954) Assam—Continuous line and open circles. London.—Broken line and squares.

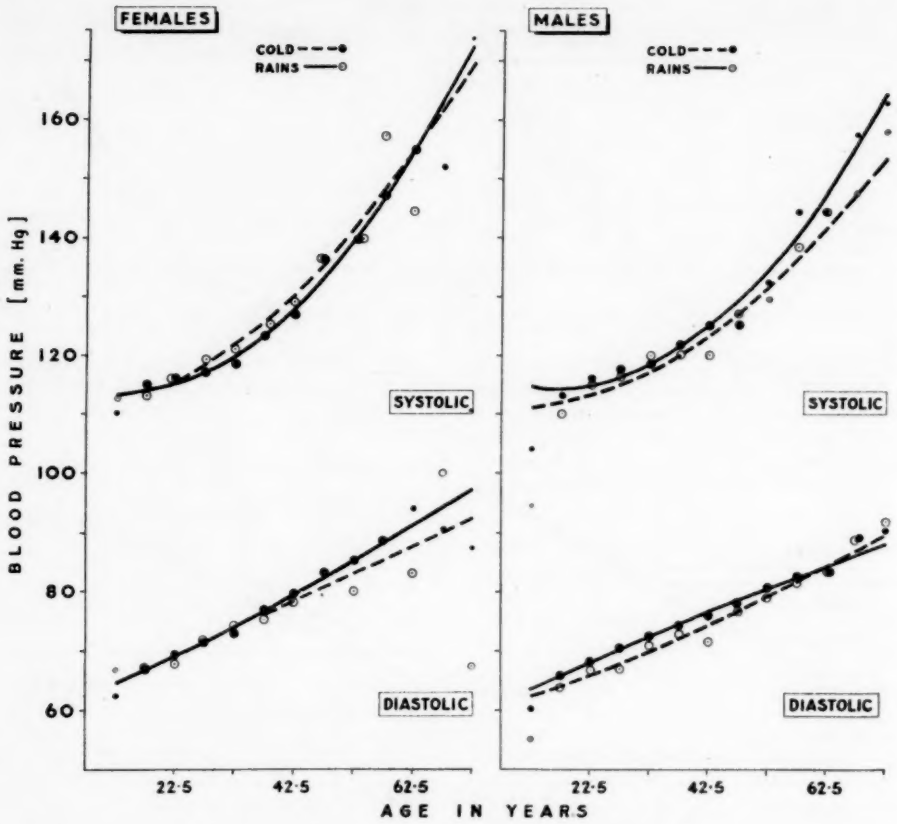
Note: the London curves are fitted from cubic equations.

No comparable clinical observations are known to the writer; the blood pressure is usually regarded as being lower in tropical countries, as already noted. After periods of experimental exposure to heat the systolic and diastolic blood pressure in human subjects at rest falls (Hellon and Lind, 1958). It may well be that the Indian workman is particularly well adapted to his environment; or some other variable, such as diet, may account for the lack of climatic variation.

Thus it appears that this Indian population, despite wide variations from Western standards of diet, climate, physique, and general environment, shows the same blood pressure trends as the population of London. It has also been demonstrated (to be published) that the frequency distribution of blood pressure in each age group follows the characteristics of a continuous variable, as reported by Hamilton and others (1954), without any line of demarcation between the normotensive and the hypertensive state.

SUMMARY

Observations on the arterial blood pressure in tea plantation workers in North East India have shown that, despite the difference from Western standards of diet, climate, physique, and general environment, the findings show similar trends to those represented for the population of London.



FIGS 5 and 6.—Rise in arterial blood pressure with age in men and women tea-garden labourers in Assam, compared for cold weather winter season and monsoon rainy season.
Winter—Broken line and solid circles. Monsoon—Continuous line and open circles.

APPENDIX

Correction of Arterial Pressure for Arm Circumferences

From Ragan and Bordley's data, Pickering and others (1954) have calculated equations relating arm size to indirect sphygmomanometric blood pressure recording and direct intra-arterial measurement. They do not give actual arm measurements but, applying their equations, the mid-arm measurement at mean age 45 years would be approximately 25·4 cm. for women and 25·6 cm. for men. The corresponding Indian measurements are 21·4 cm. and 23·4 cm. respectively. Applying these workers' correction factor (Table I in the above paper), the intra-arterial pressure would be 10 mm. Hg higher than the indirect systolic Blood Pressure reading in the Assam series, but only 5 mm. Hg higher in the London measurements. This would tend to minimize the difference between the two systolic curves.

For the diastolic measurement the same correction of 5 mm. Hg is applicable in both series. However, these deductions must be accepted with some reserve: in the first place, Pickering's arm measurements were taken half-way along the length of the arm, with forearm extended; whilst the Assam measurements were simply recorded as mid-biceps: and secondly, the calculation of Pickering's 45-year-old subjects' arm circumference is based on mean blood pressures at that age. It would be more satisfactory to compare age specific blood pressures corrected for arm circumference.

It is a pleasure to acknowledge the help given me in this by Dr. D. C. Majumdar, and also by Drs. N. L. Pal, A. C. Biswas, S. M. Chaudhury, A. Chaudhuri, T. C. Das, N. Das, B. C. Das Gupta, M. A. Rahman, G. Sarma, B. L. Sen, A. Sen Gupta, T. Sonowal, and K. Bhattacharjee.

REFERENCES

Alam, G. M., and Smirk, F. H. (1943). *Brit. Heart J.*, **5**, 152.
Bibile, S. W., Cullumbine, H., Kirtisinghe, C., Watson, R. S., and Wikramanayake, T. (1949). *Ceylon J. med. Sci.* (D), **6**, 79.
Cadbury, W. W., (1922). *Arch. intern. Med.*, **30**, 362.
Chopra, R. N., Chopra, G. S., and Chopra, I. C. (1942). *Indian med. Gaz.*, **77**, 21.
Foster, J. H. (1927). *Arch. intern. Med.*, **40**, 38.
Hamilton, M., Pickering, G. W., Roberts, J. A. Fraser, and Sowry, G. S. C., (1954). *Clin. Sci.*, **13**, 11.
Hellon, R. F., and Lind, A. R. (1958) *J. Physiol.* (*Lond.*), **141**, 262
Kilborn, L. G. (1926). *China med. J.*, **40**, 1.
Master, A. M., Dublin, L. I., and Marks, H. H. (1950). *J. Amer. med. Ass.*, **143**, 1464.
Munro, A. F. (1949). *J. Physiol.* (*Lond.*), **110**, 356.
Ordman, B., (1948). *Clin. Proc.*, **7**, 183.
Pickering, G. W., Roberts, J. A. Fraser, and Sowry, G. S. C. (1954). *Clin. Sci.*, **13**, 267.
Tung, C. L. (1927). *Arch. intern. Med.*, **40**, 153.
—— (1930). *Chin. J. Physiol.*, **4**, 117.
Williams, A. W. (1941). *East Afr. med. J.*, **18**, 109.

INDEX TO VOLUME XII, 1958

Abnormalities, genetic determinant of, 183
ACHESON, E. D., *See* ACHESON, R. M., and ACHESON, E. D.
ACHESON, R. M., and ACHESON, E. D.: Coronary and other heart disease in a group of Irish males aged 65-85, 147
— and THORNTON, E. H.: Mortality from coronary artery disease and "myocardial degeneration" in the Republic of Ireland, 82
ADAMS, J. C. S., *See* SPRINGETT, V. H., ADAMS, J. C. S., D'COSTA T. B., and HEMMING, M.
Air pollution and other local factors in respiratory disease, 94
Anencephalus in Scotland, 115
Army, British, gastric and duodenal ulcer in, 71
Atmospheric pollution and mortality in the County of London, 104

BARON, J. H., and JONES, R. V.: Incidence of gastric and duodenal ulcer in the British army in 1955, 71
BARR, A.: The extent of hospital sickness, 61
—: Hospital size and staff sickness rates, 156
Birmingham, post-neonatal infant mortality in, 1947-1956, 131
— tuberculosis in immigrants in, 1956-1957, 135
Birth order of psychiatric patients, 43
Blood pressure in Indian plantation workers, 204
British Army, gastric and duodenal ulcer in, 71

CARTWRIGHT, A., and JEFFERYS, M.: Married women who work: their own and their children's health, 159
Central nervous system, congenital malformations of, in Scotland, 115
Chicken pox, maternal, and congenital defects, 1
Child health and the working mother, 159
Children of married women who work, 159
CIOCCO, A., *See* THOMPSON, D. J., and CIOCCO, A.
Colour blindness, pedigree data of gene frequency for, 193
Congenital defects and virus diseases in pregnancy, 1
— dislocation of the hip, environmental influences related to, 8
— malformations of the central nervous system in Scotland, 115
— pyloric stenosis, determinants of, 188
Coronary and other heart disease in Irish males aged 65–85, 147
— artery disease in republic of Ireland, 82

D'COSTA, T. B., *See* SPRINGETT, V. H., ADAMS, J. C. S., D'COSTA, T. B., and HEMMING, M.
Death rates, new method of standardizing, 154
—, sickness, change of residence, and, 172
Determinants of congenital pyloric stenosis, 188
DOLL, R., *See* HILL, A. B., DOLL, R., GALLOWAY, T. MCL., and HUGHES, J. P. W.
Duodenal and gastric ulcer in the British Army in 1955, 71

EDWARDS, J. H.,: Congenital malformations of the central nervous system in Scotland, 115
—: A note on the interpretation of $n \times 2$ tables, 141
—, *See also* RECORD, R. G., and EDWARDS, J. H.
England and Wales, seasonal swing in mortality in, 197
Environmental influences related to aetiology of congenital dislocation of the hip, 8

FAIRBAIRN A. S., and REID, D. D.: Air pollution and other local factors in respiratory disease, 94
Familial data on psychiatric patients, analysis of, 42

GALLOWAY, T. MCL., *See* HILL, A. B., DOLL, R., GALLOWAY, T. MCL., and HUGHES, J. P. W.
GARRATT, F. N., LOWE, C. R., and MCKEOWN, T.: Investigation of the medical and social needs of patients in mental hospitals. II. Type of accommodation and staff required, 23.
Gastric and duodenal ulcer in the British Army in 1955, 71
Gene frequency for colour blindness, 193
Genes, X-recessive, conditions determined by, 183
Genotypic frequencies among close relatives of propositi with conditions determined by X-recessive genes, 183
GORE, A. T., and SHADDICK, C. W.: Atmospheric pollution and mortality in the county of London, 104
GREGORY, I.: An analysis of familial data on psychiatric patients: parental age, family size, birth order, and ordinal position, 42

Heart disease in Irish males aged 65–85, 147
Hip, congenital dislocation of, environmental influences related to aetiology of, 8
HEMMING, M., *See* SPRINGETT, V. H., ADAMS, J. C. S., D'COSTA, T. B., and HEMMING, M.
HILL, A. B., DOLL, R., GALLOWAY, T. MCL., and HUGHES, J. P. W.: Virus diseases in pregnancy and congenital defects, 1
Hospital sickness, extent of, 61
— size and staff sickness rates, 156
HUGHES, J. P. W., *See* HILL, A. B., DOLL, R., GALLOWAY, T. MCL., and HUGHES, J. P. W.
Hydrocephalus in Scotland, 115

Immigrants in Birmingham, tuberculosis in, 135
Indian plantation workers, blood pressure in, 204
Infant mortality, post-neonatal, in Birmingham, 1947–1956, 131
Inheritance of abnormalities, 183
Insured population of Northern Ireland, morbidity in, 75
Ireland, Northern, morbidity in insured population of, 75
—, Republic of, coronary artery disease and "myocardial degeneration" in, 82
Irish males aged 65–85, coronary and other heart disease in, 147

JEFFERYS, M., *See* CARTWRIGHT, A., and JEFFERYS, M.
JONES, R. V., *See* BARON, J. H., and JONES, R. V.

KANELLAKIS, A. P.: Seasonal swing in mortality in England and Wales, 197
KERRIDGE, D.: A new method of standardizing death rates, 154
KIDD, C. W., *See* PARK, A. T., and KIDD, C. W.
KNOX, G.: An estimate from pedigree data of the gene frequency for colour blindness, 193
—: Genotypic frequencies among close relatives of propositi with conditions determined by X-recessive genes, 183
—: On the nature of the determinants of congenital pyloric stenosis, 188
— and MACKINTOSH, J.: Post-neonatal infant mortality in Birmingham between 1947 and 1956, 131

London, County of, atmospheric pollution and mortality in, 104
LOWE, C. R., *See* GARRATT, F. N., LOWE, C. R., and MCKEOWN, T.

MCKEOWN, T., *See* GARRATT, F. N., LOWE, C. R., and MCKEOWN, T.
MACKINTOSH, J., *See* KNOX, G., and MACKINTOSH, J.
Married women, working, 159
Measles, maternal, and congenital defects, 1
Mental hospitals, medical and social needs of patients in, 23
— —,type of accommodation and staff required, 23
Morbidity in insured population of Northern Ireland, 75
— studies based on hospital admission rates, 61
Mortality in England and Wales, seasonal swing, 197
—, infant, in Birmingham, 131
— rates, new method of standardizing, 154
— — and change of residence, 172
Mumps, maternal, and congenital defects, 1
"Myocardial degeneration" in Republic of Ireland. 82

$n \times 2$ tables, interpretation of, 141
Northern Ireland, morbidity in insured population of, 75

Parental age and psychiatric disorders, 43
PARK, A. T., and KIDD, C. W.: Morbidity in the insured population of northern Ireland, 75
Pedigree data of gene frequency for colour blindness, 193
Peptic ulcer in the British Army in 1955, 71
Post-neonatal infant mortality in Birmingham between 1947 and 1956, 131
Pregnancy, virus diseases in, and congenital defects, 1
Psychiatric patients, analysis of familial data on, 42
Pyloric stenosis, congenital, determinants of, 188

RECORD, R. G., and EDWARDS, J. H.: Environmental influences related to the aetiology of congenital dislocations of the hip, 8
REID, D. D., *See* FAIRBAIRN, A. S., and REID, D. D.
Residence changes and mortality rates, 172
Respiratory disease, air pollution and other local factors in, 94
Rubella, maternal, and congenital defects, 1

Scotland, congenital malformations of central nervous system in, 115
Seasonal changes in blood pressure in Indian plantation workers, 204
— swing in mortality in England and Wales, 197
SHADDICK, C. W., *See* GORE, A. T., and SHADDICK, C. W.
Sickness, change of residence, and death, 172
— rates of hospital staffs, 156
Social needs of patients in mental hospitals, 23
Spina bifida in Scotland, 115
SPRINGETT, V. H., ADAMS, J. C. S., D'COSTA, T. B., and HEMMING, M.: Tuberculosis in immigrants in Birmingham, 1956–1957, 135
Staff sickness rates and hospital size, 156

THOMPSON, D. J., and CIOCCO, A.: Sickness, change of residence, and death. I. General results of follow-up in two population groups, 172
THORNTON, E. H., *See* ACHESON, R. M., and THORNTON, E. H.
Trend, analysis of, 141
Tuberculosis in immigrants in Birmingham, 1956–1957, 135

Virus diseases in pregnancy and congenital defects, 1

WILSON, J. M. G.: Arterial blood pressure in plantation workers in N.E. India, 204
Women who work: their own and their children's health, 159

X-recessive genes, genotypic frequencies among close relatives of propositi with conditions determined by, 183

For their tomorrows

Today it's play. Tomorrow, perhaps, comes the challenge of the workaday world and with it the greater risk of contracting tuberculosis. To make it easier to reduce the danger of this disease to a minimum Glaxo have worked for many years to perfect a safe, potent, standardized British freeze-dried B.C.G. vaccine that can be administered to school-leavers, infants and others needing special protection. Time or place impose no restrictions on the use of this product—it has a life of at least 12 months and can, if necessary, be transported to the ends of the earth.

Glaxo Products for Protection

FREEZE-DRIED B.C.G. VACCINE
POLIVIRIN *the first British poliomyelitis vaccine*
INFLUENZA VIRUS A *(Asian) Vaccine*
TRIPLE ANTIGEN *(Diphtheria-Tetanus-Pertussis Prophylactic) and separate antigens*

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX BYRon 3434
Subsidiary Companies or Agents in most countries

INDUSTRIAL CLEANLINESS

SAROUL

gives 24 hour protection to hands and skin

Adequate protection is ensured by using Saroul after work—it is scientifically compounded to remove grime and dirt quickly and completely. It is not a harsh antiseptic but a cleansing agent which assists the natural healing processes and extends its protective effect for many hours. Saroul is a positive safeguard against industrial dermatitis.

Testing samples and literature free on request to Dept. CS.

SAROUL Antiseptic Hand Cleanser is made by

Sandeman Brothers Ltd.

BILSLAND DRIVE · MARYHILL . GLASGOW

J. & A. CHURCHILL LTD.

New (Eleventh) Edition.

A SYNOPSIS OF HYGIENE
(Jameson & Parkinson)
By LLYWELYN ROBERTS, M.D., M.R.C.P., D.P.H , assisted by KATHLEEN M. SHAW, *M.B.E.*
22 Illustrations — 60s.

Ready this month

PUBLIC HEALTH PRACTICE IN TROPICAL COUNTRIES
By OLADELE A. AJOSE, M.D., D.P.H.
25 Illustrations — 18s.

PRINCIPLES OF EPIDEMIOLOGY
By IAN TAYLOR, M.D., M.R.C.P., D.P.H., and JOHN KNOWELDEN, M.D., D.P.H.
25 Illustrations — 30s.

THE EXAMINATION OF WATERS AND WATER SUPPLIES
(Thresh, Beale & Suckling)
By E. WINDLE TAYLOR, M.A., M.D., M.R.C.S., D.P.H.
New (Seventh) Edition. 51 Illustrations. — 100s.

INFANT FEEDING AND FEEDING DIFFICULTIES
By P. R. EVANS, M.D., F.R.C.P., and RONALD MacKEITH, D.M., F.R.C.P. *New (Third) Edition.*
66 Illustrations, including 2 colour plates. — 16s.

MEDICAL BACTERIOLOGY
Including Elementary Mycology and Parasitology
By SIR LIONELWHITBY, *C.V.O.*, M.A., M.D., F.R.C.P., D.P.H., and MARTIN HYNES, M.D., F.R.C.P.
Sixth Edition. 103 Illustrations. — 30s.

DISEASES OF INFANCY AND CHILDHOOD
By WILFRID SHELDON, *C.V.O.*, M.D., F.R.C.P.
Seventh Edition. 213 Text-figures and including 18 Plates (5 in colour). — 50s.

THE PRACTICE OF INDUSTRIAL MEDICINE
By T. A. LLOYD DAVIES, M.D., F.R.C.P.
New (Second) Edition. 15 Illustrations — 30s.

Ciba Foundation COLLOQUIA ON AGEING

Vol. 2. **Ageing in Transient Tissues**
96 Illustrations. — 30s.

Vol. 3. **Methodology in the Study of Ageing**
46 Illustrations. — 32s. 6d.

Vol. 4. **Water and Electrolyte Metabolism in Relation to Sex and Age**
85 Illustrations — 45s.

THE HEALTH OF THE COMMUNITY
Principles of Public Health for Practitioners and Students
By C. FRASER BROCKINGTON, M.A., M.D., M.R.C.S., D.P.H. — 32s.
By the same author:
A SHORT HISTORY OF PUBLIC HEALTH — 15s.

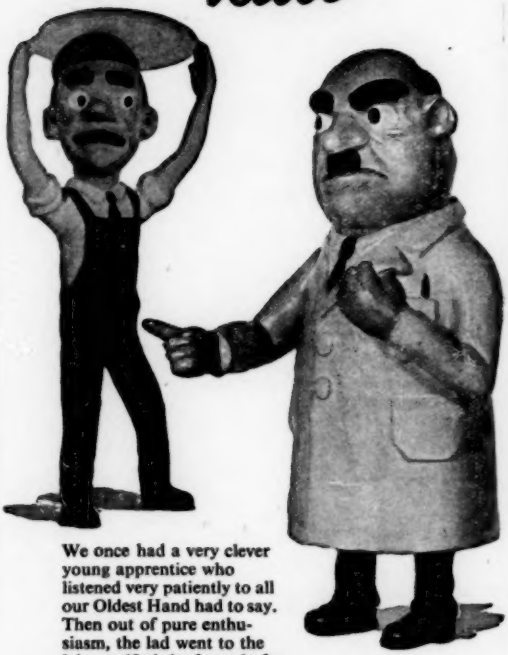
From U.S.A.

B.C.G. VACCINATION AGAINST TUBERCULOSIS
By SOL ROY ROSENTHAL, M.D., Ph.D.
With 43 Illustrations and 28 Tables. — 55s.

PROLONGED AND PERPLEXING FEVERS
By CHESTER S. KEEFER, M.D., and SAMUEL E. LEARD, M.D. — 42s.

104 GLOUCESTER PLACE, LONDON, W.1

Hexachlorophene halo



We once had a very clever young apprentice who listened very patiently to all our Oldest Hand had to say. Then out of pure enthusiasm, the lad went to the lab., verified the formula for our barrier cream, and finally announced:

"What you tell me about Hexachlorophene is absolutely right. It really is such a fine protection against bacteria. I shall use nothing else but Sternocleanse from now on to guard against dermatitis!"

Speechless, our O.H. patted the lad's head. Then he tottered away, muttering:

"I wash my 'ands of 'im,
I really do . . . ."

Sternol

Sternocleanse barrier cream

STERNOL LIMITED
ROYAL LONDON HOUSE
FINSBURY SQUARE, LONDON, E.C.2

E. & S. LIVINGSTONE LTD.

SCOTTISH SOCIAL WELFARE, 1864–1914
By THOMAS FERGUSON, C.B.E., M.D., D.Sc., F.R.C.P.Ed., F.R.F.P.S.G., D.P.H., F.R.S.Ed.
622 pages 22 illustrations 42s.

ANTISERA, TOXOIDS, VACCINES AND TUBERCULINS IN PROPHYLAXIS AND TREATMENT
Fourth Edition. By H. J. PARISH, M.D., F.R.C.P.E., D.P.H.
266 pages 50 illustrations 30s.

LEPTOSPIROSIS IN MAN AND ANIMALS
By J. M. ALSTON, M.D., F.R.C.P.Ed., and JOHN C. BROOM, *O.B.E.*, M.D.
380 pages 40 illustrations 40s.

NON-VENEREAL SYPHILIS
A Sociological and Medical Study of Bejel
By E. HERNDON HUDSON, M.D., D.T.M. & H., F.A.C.P.
212 pages 106 illustrations 30s.

USES OF EPIDEMIOLOGY
By J. N. MORRIS, M.A., F.R.C.P., D.P.H.
143 pages 28 illustrations 17s. 6d.

TEXTBOOK OF MEDICAL TREATMENT
Seventh Edition. Edited by D. M. DUNLOP, M.D., F.R.C.P., SIR STANLEY DAVIDSON, M.D., F.R.C.P., and S. ALSTEAD, M.D., F.R.C.P.
944 pages 33 illustrations 55s.

TEVIOT PLACE, EDINBURGH

READY SHORTLY

RHEUMATIC FEVER
Epidemiology and Control
Edited by
R. CRUICKSHANK AND A. A. GLYNN

This Symposium was organized by the International Children's Centre in Paris, and brought together a number of epidemiologists, bacteriologists, paediatricians, and rheumatologists from eighteen countries. Their papers and discussions will be of interest to all who are concerned with the control of rheumatic fever.

224 pages 5 illustrations About 25s.

RECENT STUDIES IN EPIDEMIOLOGY
Edited by
J. PEMBERTON AND H. WILLARD

All the papers included in this book were presented at the Study Group on Current Epidemiological Research held in Holland in September 1957. The aim was to assemble information on the ways in which epidemiological methods are being used in different parts of the world to investigate the incidence and causation of disease and to assess the needs of communities for various health services. The result is a practical handbook on epidemiological methods which describes the way in which epidemiological studies can be carried out, the sort of difficulties which have to be overcome, and some results that have been obtained.

224 pages 21 illustrations 25s.

BLACKWELL SCIENTIFIC PUBLICATIONS

EMERGENCIES IN GENERAL PRACTICE

This book comprises 57 specially commissioned articles on medical emergencies which appeared originally in the *British Medical Journal*.

Contents include haemorrhage and thrombosis, cardio-respiratory crises, anaesthesia and hazards of therapy, acute abdominal cases, obstetrics, fits and coma, electrocution, burns and gassing, poisoning, acute psychiatric states, and special and minor surgery.

Invaluable to all doctors everywhere.

470 *pages, cloth bound with full index.* 25*s. net* (*by post—inland and overseas* 26*s.* 9*d.*).

CLINICAL PATHOLOGY IN GENERAL PRACTICE

This handbook on clinical pathology meets the needs of the general practitioner, the houseman, and the senior student. It contains thirty-nine articles comprising a series specially written for the *British Medical Journal*. Each article has been revised and brought up-to-date by its author. The book gives authoritative information on available laboratory facilities; reliable tests and which to use; techniques for collecting and preserving specimens; interpretation of results and significance of abnormal findings.

321 *pages. Price* 21*s.* (*by post—inland and overseas* 22*s.* 3*d.*)

REFRESHER COURSE FOR GENERAL PRACTITIONERS

Second Collection

Third Collection—with Classified Contents List to volumes 1, 2 and 3

Each book contains a collection of sixty Refresher Course articles from the *British Medical Journal*. Each article, written by an acknowledged expert, has been revised by its author. The articles cover a wide range. Their object is to refresh the reader's memory of what is old and well-established and to tell him about new developments.

They are invaluable to general practitioners and residents as practical reference books, to specialists as a means of keeping in touch with developments outside their own field, and to final-year students as up-to-date and reliable textbooks.

25*s. each* (*by post—inland and overseas* 26*s.* 9*d.*)

"ANY QUESTIONS?"

Second Series

Third Series—with Cumulative Index

These pocket-size volumes each contain some 200 questions and expert answers from the "Any Questions?" pages of the *British Medical Journal*. Each answer has been chosen for its practical value to doctors in their day-to-day work. Many deal with subjects not covered in the standard textbooks.

The Third volume has a cumulative index to all the answers appearing in the three books in the series.

7*s.* 6*d. each* (*by post* 8*s.* 3*d.*)

Obtainable from booksellers or by post from

BRITISH MEDICAL ASSOCIATION

B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1

7633

PRINTED IN GREAT BRITAIN BY GEO. GIBBONS., LTD AYLESTONE ROAD, LEICESTER